PCT$

TRANSMITTAL LETTER TO THE UNITED STATES ATTORNEY'S DOCKET NUMBER 50761

DESIGNATED/ELECTED OFFICE (DO/EO/US)
CONCERNING A FILING UNDER 35 U.S.C. 371 U S APPLICATION NO (If known, see 37 CFR 1 5)

INTERNATIONAL APPLICATION NO	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/EP00/09023	**15 September 2000**	**28 September 1999**

TITLE OF INVENTION: BENZODIAZEPINE DERIVATIVES, THE PREPARATION AND USE THEREOF

APPLICANT(S) FOR DO/EO/US Wilfried LUBISCH, Michael KOCK, Thomas HOEGER, Roland GRANDEL, Reinhold MUELLER, Sabine SCHULT

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information

1. /X/ This is a FIRST submission of items concerning a filing under 35 U S C 371

2. / / This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U S C 371

3. /X/ This express request to begin national examination procedures (35 U.S.C 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U S.C 371(b) and PCT Articles 22 and 39(1)

4. /x / A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date

5. /X/ A copy of the International Application as filed (35 U.S.C 371(c)(2)).

   a./X/ is transmitted herewith (required only if not transmitted by the International Bureau)
   b./ / has been transmitted by the International Bureau.
   c / / is not required, as the application was filed in the United States Receiving Office (RO/US0)

6. /X/ A translation of the International Application into English (35 U S C 371(c)(2))

7. / / Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C 371(c)(3)).

   a / / are transmitted herewith (required only if not transmitted by the International Bureau)
   b / / have been transmitted by the International Bureau
   c / / have not been made, however, the time limit for making such amendments has NOT expired
   d./ / have not been made and will not be made

8. / / A translation of the amendments to the claims under PCT Article 19(35 U.S.C. 371(c)(3)).

9. / / An oath or declaration of the inventor(s)(35 U S.C. 171(c)(4))

10./ / A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U S C 371(c)(5))

Items 11. to 16. below concern other document(s) or information included

11./ / An Information Disclosure Statement under 37 CFR 1.97 and 1 98

12./ / An assignment document for recording A separate cover sheet in compliance with 37 CFR 3 28 and 3.31 is included.

13./X / A FIRST preliminary amendment.
/ / A SECOND or SUBSEQUENT preliminary amendment

14./ / A substitute specification

15./ / A change of power of attorney and/or address letter.

16./x / Other items or information
International Search Report
International Preliminary Examination Report

[redacted]

U S. Appln. No. (If Known)	INTERNATIONAL APPLN NO. PCT/EP00/09023	ATTORNEY'S DOCKET NO 50761

17. /X/ The following fees are submitted	CALCULATIONS	PTO USE ONLY
BASIC NATIONAL FEE (37 CFR 1.492(a)(1)-(5)): Search Report has been prepared by the EPO or JPO..... .. .. $890.00	**890.00**	
International preliminary examination fee paid to USPTO (37 CFR 1.482).. .... $710.00		
No international preliminary examination fee paid to USPTO (37 CFR 1.482) but international search fee paid to USPTO (37 CFR 1 445(a)(2))..... .... $740 00		
Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO ....$ 1,040.00		
International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied pro -visions of PCT Article 33(2)-(4).... .. . .$100.00		
ENTER APPROPRIATE BASIC FEE AMOUNT =	$ 890.00	
Surcharge of $130.00 for furnishing the oath or declaration later than / / 20 / /30 months from the earliest claimed priority date (37 CFR 1.492(e)).		

Claims	Number Filed		Number Extra	Rate	
Total Claims	26	-20	6	X$18. 108.00	
Indep.Claims	3	-3		X$84.	
Multiple dependent claim(s)(if applicable)				+280	
TOTAL OF ABOVE CALCULATION				= **998.**	
Reduction of 1/2 for filing by small entity, if applicable. Verified Small Entity statement must also be filed (Note 37 CFR 1 9, 1.27, 1.28).					
SUBTOTAL				= 998	
Processing fee of $130. for furnishing the English translation later than / /20 / /30 months from the earliest claimed priority date (37 CFR 1.492(f)).				+	
TOTAL NATIONAL FEE				= **998 .**	
Fee for recording the enclosed assignment (37 CFR 1.21(h)) The assignment must be accompanied by an appropriate cover sheet (37 CFR 3 28, 3 31) $40.00 per property				=	
TOTAL FEES ENCLOSED				= **$ 998.00**	
				Amount to be refunded: $	
				Charged $	

a./X/ A check in the amount of $ 998.00 to cover the above fees is enclosed

b./ / Please charge my Deposit Account No._____in the amount of $_____ to cover the above fees. A duplicate copy of this sheet is enclosed

c./X/ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No **11-0345**. A duplicate copy of this sheetis enclosed

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:
KEIL & WEINKAUF
1101 Connecticut Ave., N.W
Washington, D. C. 20036

Herbert B. Keil
SIGNATURE

Herbert B Keil
NAME
Registration No. 18,967

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of)
LUBISCH et al.) BOX PCT
)
International Application)
PCT/EP 00/09023)
)
Filed: September 16, 2000)
)

For: BENZODIAZEPINE DERIVATIVES, THE PREPARATION AND USE THEREOF

PRELIMINARY AMENDMENT

Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

Sir:

Prior to examination, kindly amend the above-identified application as follows:

IN THE CLAIMS

Kindly amend the claims as shown on the attached sheets.

REMARKS

The claims have been amended to eliminate multiple dependency and to place them in better form for U.S. filing. No new matter is included.

A clean copy of the claims is attached.

Favorable action is solicited.

Respectfully submitted,

KEIL & WEINKAUF

/HBKeil

Herbert B. Keil
Reg. No. 18,967

1101 Connecticut Ave., N.W.
Washington, D.C. 20036

(202)659-0100

CLEAN VERSION OF AMENDED CLAIMS - OZ 50761

3. A compound of the formula I as claimed in claim 1, in which

B can be an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 15 carbon atoms, an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 14 carbon atoms and 0 to 5 nitrogen atoms, 0 to 2 oxygen atoms or 0 to 2 sulfur atoms, each of which may also be substituted by a maximum of 3 different or identical R^5 radicals, and one or two carbon or sulfur atoms may also carry one or two =O groups.

6. A compound of the formula I as claimed in claim 1, in which B is L_v-Y-M_w, where

v is 0, and

w is 1, and

Y is a bond, and

M can be a straight-chain or branched carbon chain of 2 to 8 C atoms which contains at least one double bond, it being possible for each carbon atom to be substituted by one or two R^4 radicals and a maximum of two different or identical R^5 radicals, and

R^1 is hydrogen, and

R^4 is $D_{0,1}$-$F^1_{0,1}$-G^1-G^2-G^3, with G^3 equal to hydrogen, and

D is O and NR^{43}, where R^{43} is hydrogen and C_1-C_3-alkyl and

F^1 is C_2-C_4-alkyl.

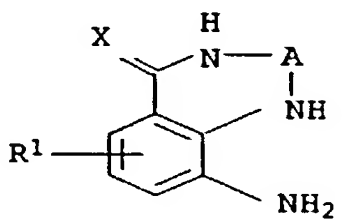
7. A drug comprising one or more compounds of the formula I as claimed in claim 1 in addition to conventional carriers and excipients.

[redacted]

CLEAN VERSION OF AMENDED CLAIMS - OZ 50761

8. The use of compounds of the formula I as claimed in claim 1 or of the formula I where R^1, X^1 and A have the meaning as above, and B can be hydrogen and a C_1-C_6-alkyl chain, for producing drugs with a PARP-inhibiting effect.

24. A compound of the formula III



III

in which

A is a C_1-C_3 chain it being possible for each carbon atom also to carry one or two of the following substituents: C_1-C_4-alkyl, OH, O-C_1-C_4-alkyl, CO_2H, Co_2-C_1-C_4-alkyl and phenyl or one C atom may also carry an =O group, and

X^1 and R^1 have the meanings stated in claim 1,

excluding the compounds

9-amino-3-methyl-1,2,3,4-tetrahydro-5H-1,4-benzodiazepin-5-one,

9-amino-3-methyl-3,4-dihydro-1H-1,4-benzodiazepine-2,5-dione,

6,8-diamino-2,4-(1H,3H)-quinazolinedione,

8-amino-2,4-(1H,3H)-quinazolinedione,

and the salts thereof.

MARKED VERSION OF AMENDED CLAIMS - OZ 50761

3. A compound of the formula I as claimed in claim 1 [either of claims 1 or 2], in which

B can be an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 15 carbon atoms, an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 14 carbon atoms and 0 to 5 nitrogen atoms, 0 to 2 oxygen atoms or 0 to 2 sulfur atoms, each of which may also be substituted by a maximum of 3 different or identical R^5 radicals, and one or two carbon or sulfur atoms may also carry one or two =O groups.

6. A compound of the formula I as claimed in claim 1 [either claims 1 or 2], in which

B is L_v-Y-M_w, where

v is 0, and

w is 1, and

Y is a bond, and

M can be a straight-chain or branched carbon chain of 2 to 8 C atoms which contains at least one double bond, it being possible for each carbon atom to be substituted by one or two R^4 radicals and a maximum of two different or identical R^5 radicals, and

R^1 is hydrogen, and

R^4 is $D_{0,1}$-$F^1_{0,1}$-G^1-G^2-G^3, with G^3 equal to hydrogen, and

D is O and NR^{43}, where R^{43} is hydrogen and C_1-C_3-alkyl and

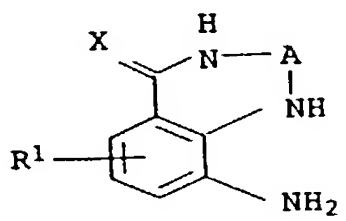
F^1 is C_2-C_4-alkyl.

MARKED VERSION OF AMENDED CLAIMS - OZ 50761

7. A drug comprising one or more compounds of the formula I as claimed in claim 1 [any of claims 1 to 6] in addition to conventional carriers and excipients.

8. The use of compounds of the formula I as claimed in claim 1 [any of claims 1 to 6] or of the formula I where R^1, X^1 and A have the meaning as above, and B can be hydrogen and a C_1-C_6-alkyl chain, for producing drugs with a PARP-inhibiting effect.

24. A compound of the formula III



III

in which

A is a C_1-C_3 chain it being possible for each carbon atom also to carry one or two of the following substituents: C_1-C_4-alkyl, OH, O-C_1-C_4-alkyl, CO_2H, Co_2-C_1-C_4-alkyl and phenyl or one C atom may also carry an =O group, and

X^1 and R^1 have the meanings stated in claim 1 [the previous claims],

excluding the compounds

9-amino-3-methyl-1,2,3,4-tetrahydro-5H-1,4-benzodiazepin-5-one,

9-amino-3-methyl-3,4-dihydro-1H-1,4-benzodiazepine-2,5-dione,

MARKED VERSION OF AMENDED CLAIMS - OZ 50761

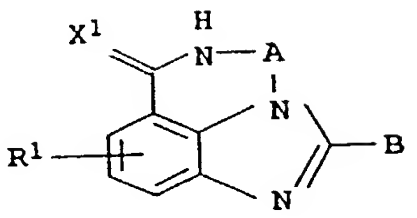
6,8-diamino-2,4-(1H,3H)-quinazolinedione,

8-amino-2,4-(1H,3H)-quinazolinedione,

and the salts thereof.

CLAIMS AS FILED - OZ 50761

1. A compound of the formula I



I

in which

A can be a C_1-C_3 chain where each carbon atom may also carry one or two of the following substituents:

C_1-C_4-alkyl, OH, O-C_1-C_4-alkyl, COOH, COO-C_1-C_4-alkyl and phenyl or

one C atom may also carry an =O group, and

X^1 can be S, O and NH, and

R^1 is hydrogen, chlorine, fluorine, bromine, iodine, branched and unbranched C_1-C_6-alkyl, OH, nitro CF_3, CN, $NR^{11}R^{12}$, NH-CO-R^{13}, O-C_1-C_4-alkyl, where R^{11} and R^{12} are, independently of one another, hydrogen, or C_1-C_4-alkyl, and R^{13} is hydrogen, C_1-C_4-alkyl, C_1-C_4-alkyl-phenyl or phenyl, and

B can be an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 15 carbon atoms, an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 14 carbon atoms and 0 to 5 nitrogen atoms, 0 to 2 oxygen atoms or 0 to 2 sulfur atoms, each of which may also be substitued by one R^4 and a maximum of 3 different or identical R^5 radicals, and one or two carbon or sulfur atoms may also carry one or two =O groups, or is a radical L_v-Y-M_w in which

L can be a straight-chain or branched, saturated or unsaturated carbon chain of 1

CLAIMS - OZ 50761

to 8 C atoms, it being possible for each carbon atom to be substituted by one or two R^4 radicals and a maximum of two different or identical R^5 radicals, and

M has, independently of L, the same meaning as L, and

Y is a bond, or can be S, O or NR^3, where R^3 can be hydrogen, branched and unbranched C_1-C_6-alkyl, C_1-C_4-alkyl-phenyl, phenyl, and

v can be 0 and 1, and

w can be 0 and 1, and

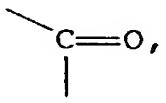
when Y is a bond, R^4 and R^5 are not both hydrogen, and

when B is L_v-Y-M_w , R^1 is not chlorine or NO_2 and

R^4 is hydrogen and -$(D)_p$-$(E)_s$-$(F^1)_q$ -G^1-$(F^2)_r$-(G^2)-G^3, where

D can be S, NR^{43} and O

E can be phenyl,



, -SO_2-, -SO_2NH-, -NHCO-, -CONH-, $NHSO_2$,

-$NHCOCH_2X^4$

and

X^4 can be S, O or NH, and

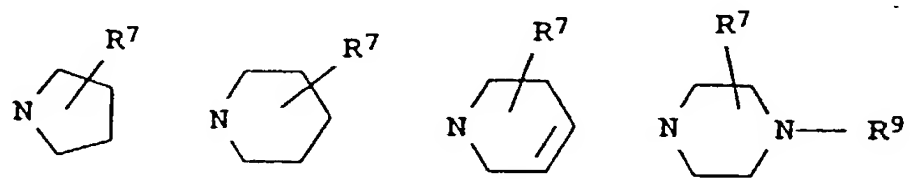
F^1 can be a straight-chain or branched saturated or unsaturated carbon chain of 1 to 8 C atoms, and

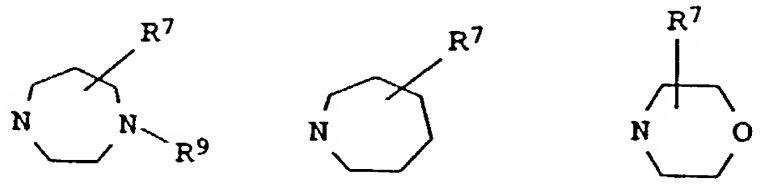
F^2 has, independently of F^1, the same meaning as F^1,

CLAIMS - OZ 50761

G^1 is a bond or can be an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 15 carbon atoms, an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 14 carbon atoms and 0 to 5 nitrogen atoms, 0 to 2 oxygen atoms or 0 to 2 sulfur atoms, each of which may also be substituted by a maximum of 3 different or identical R^5 radicals, and one or two carbon or sulfur atoms may also carry one or two =O groups, and

G^2 is $NR^{41}R^{42}$ and





or a bond, and

G^3 can be an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 15 carbon atoms, an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 14 carbon atoms and 0 to 5 nitrogen atoms, 0 to 2 oxygen atoms or 0 to 2 sulfur atoms, each of which may also be substituted by a maximum of 3 different or identical radicals R^5, and one or two carbon or sulfur atoms may also carry one or two =O groups, or is

CLAIMS - OZ 50761

hydrogen, and

p can be 0 and 1 and

s can be 0 and 1 and

q can be 0 and 1 and

r can be 0 and 1 and

R^{41} can be hydrogen C_1-C_6-alkyl, it being possible for each carbon atom also to carry up to two R^6 radicals, phenyl which may also carry a maximum of two R^6 radicals, and $(CH_2)_t$-K and

R^{42} can be hydrogen, C_1-C_6-alkyl, -CO-R^8, CO_2-R^8, SO_2NH_2, SO_2-R^8, -(C=NH)-R^8 and -(C=NH)-NHR^8 and

R^{43} can be hydrogen and C_1-C_4-alkyl and

t can be 1, 2, 3, 4 and

K can be $NR^{11}R^{12}$, NR^{11}-C_1-C_4-alkyl-phenyl, pyrrolidine, piperidine, 1,2,5,6-tetrahydropyridine, morpholine, homopiperidine, piperazine, which may also be substituted by an alkyl radical C_1-C_6-alkyl, and homopiperazine which may also be substituted by an alkyl radical C_1-C_6-alkyl, and homopiperazine which may also be substituted by an alkyl radical C_1-C_6-alkyl, and

R^5 can be hydrogen, chlorine, fluorine, bromine, iodine, OH, nitro, CF_3, CN, $NR^{11}R^{12}$, NH-CO-R^{13}, C_1-C_4-alkyl-CO-NH-R^{13}, COR^8, C_0-C_4-alkyl-O-CO-R^{13}, C_1-C_4-alkyl-phenyl, phenyl, CO_2-C_1-C_4-alkyl, and branched and unbranched C_1-C_6-alkyl, O-C_1-C_4-alkyl, S-C_1-C_4-alkyl, it being possible for each C atom of the alkyl

CLAIMS - OZ 50761

chains to carry up to two R^6 radicals, and for the alkyl chains also to be unsaturated, and,

R^6 can be hydrogen, chlorine, fluorine, bromine, iodine, branched and unbranched C_1-C_6-alkyl, OH, nitro, CF_3, CN, $NR^{11}R^{12}$, NH-CO-R^{13}, O-C_1-C_4-alkyl,

R^7 can be hydrogen, C_1-C_6-alkyl, phenyl, it being possible for the ring also to be substituted by up to two R^{71} radicals, and an amine $N^{11}R^{12}$ or a cyclic saturated amine which has 3 to 7 members and may also be substituted by an alkyl radical C_1-C_6-alkyl, and homopiperazine which may also be substituted by an alkyl radical C_1-C_6-alkyl, and homopiperazine which may also be substituted by an alkyl radical C_1-C_6-alkyl,

and where the radicals R^{11}, R^{12} and R^{13} in K, R^5, R^6 and R^7 may, independently of one another, assume the same meaning as for R^1, and

R^{71} can be OH, C_1-C_6-alkyl, O-C_1-C_4-alkyl, chlorine, bromine, iodine, fluorine, CF_3, nitro, NH_2, and

R^8 can be C_1-C_6-alkyl, CF_3, phenyl, C_1-C_4-alkyl-phenyl, it being possible for the ring also to be substituted by up to two R^{81} radicals, and

R^{81} can be OH, C_1-C_6-alkyl, O-C_1-C_4-alkyl, chlorine, bromine, iodine, fluorine, CF_3, nitro NH_2, and

R^9 can be hydrogen, C_1-C_6-alkyl, C_1-C_4-alkyl-phenyl, CO_2-C_1-C_4-alkyl-phenyl, CO_2-C_1-C_4-alkyl, SO_2-phenyl, COR^8 and phenyl, it being possible for the phenyl rings also to be substituted by up to two R^{91} radicals, and

CLAIMS - OZ 50761

R^{91} can be OH, C_1-C_6-alkyl, O-C_1-C_4-alkyl, chlorine, bromine, iodine, fluorine, CF_3, nitro, NH_2

and

its tautomeric forms, possible enantiomeric and diastereomeric forms, and prodrugs thereof.

2. A compound of the formula I as claimed in claim 1, where

A is a C_2 chain, which may be substituted, and

X^1 is O, and

R^1 is hydrogen.

3. A compound of the formula I as claimed in claim 1, in which

B can be an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 15 carbon atoms, an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 14 carbon atoms and 0 to 5 nitrogen atoms, 0 to 2 oxygen atoms or 0 to 2 sulfur atoms, each of which may also be substituted by a maximum of 3 different or identical R^5 radicals, and one or two carbon or sulfur atoms may also carry one or two =O groups.

4. A compound of the formula I as claimed in claim 3, where

B is phenyl, cyclohexyl, piperidine, pyridine, pyrimidine, pyrrole, pyrazole, thiophene, furan, oxazole, napthalene, piperazine, quinoline, pyrazine,

CLAIMS - OZ 50761

each of which may also be substituted by one R^4 or a maximum of 2 R^5.

5. A compound of the formula I as claimed in claim 4, where

R^4 is hydrogen or $D_{0,1}$-$F^1_{0,1}$-G^2-G^3 with G^3 equal to hydrogen, and

D is O and NR^{43}, where R^{43} is hydrogen and C_1-C_3-alkyl and

F^1 is C_2-C_4-alkyl.

6. A compound of the formula I as claimed in claim 1, in which B is L_v-Y-M_w, where

v is 0, and

w is 1, and

Y is a bond, and

M can be a straight-chain or branched carbon chain of 2 to 8 C atoms which contains at least one double bond, it being possible for each carbon atom to be substituted by one or two R^4 radicals and a maximum of two different or identical R^5 radicals, and

R^1 is hydrogen, and

R^4 is $D_{0,1}$-$F^1_{0,1}$-G^1-G^2-G^3, with G^3 equal to hydrogen, and

D is O and NR^{43}, where R^{43} is hydrogen and C_1-C_3-alkyl and

F^1 is C_2-C_4-alkyl.

7. A drug comprising one or more compounds of the formula I as claimed in claim 1 in addition to conventional carriers and excipients.

8. The use of compounds of the formula I as claimed in claim 1 or of the formula I where R^1, X^1 and A have the meaning as above, and B can be hydrogen and a

CLAIMS - OZ 50761

C_1-C_6-alkyl chain, for producing drugs with a PARP-inhibiting effect.

9. The use of compounds of the formula I as claimed in claim 8 for producing drugs for treating neurodegenerative disorders and neuronal damage.

10. The use as claimed in claim 8 for treating neurodegenerative disorders and neuronal damage caused by ischemia, trauma or massive bleeding.

11. The use as claimed in claim 8 for treating stroke and craniocerebral trauma.

12. The use as claimed in claim 8 for treating Alzeheimer's disease, Parkinson's disease and Huntington's disease.

13. The use of compounds of the formula I as claimed in claim 8 for producing drugs for the treatment of prophylaxis of damage due to ischemias.

14. The use of compound of the formula I as claimed in claim 8 for producing drugs for the treatment of epilepsies, in particular of generalized epileptic seizures, such as, for example, petit mal and tonoclonic seizures and partial epileptic seizures, such as temporal lobe, and complex partial seizures.

15. The use of compounds of the formula I as claimed in claim 8 for producing drugs for the treatment of damage to the kidneys after renal ischemia, damage caused by drug therapy such as, for example, during cyclosporin therapy, and for treatment during and after kidney transplants.

16. The use of compounds of the formula I as claimed in claim 8 for producing drugs for the treatment of damage to the heart following cardiac ischemia.

17. The use of compounds of the formula I as claimed in claim 8 for producing drugs

for the treatment of microinfarcts such as, for example, during and after heart valve replacement, aneurysm resections and heart transplants.

18. The use of compounds of the formual I as claimed in claim 8 for producing drugs for treatment in cases of revascularization of critically narrowed coronary arteries such as, for example in PTCA and bypass operations or of critically narrowed peripheral arteries, especially leg arteries.

19. The use of compounds of the formula I as claimed in claim 8 for producing drugs for the treatment of acute myocardinal infarct and of damage during and after medical or mechanical lysis thereof.

20. The use of compounds of the formula I as claimed in claim 8 for producing drugs for the treatment of tumors and metastasis thereof.

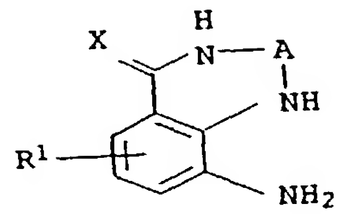
21. The use of compounds of the formula I as claimed in claim 8 for producing drugs for the treatment of sepsis, of multiorgan failure such as, for example, during septic shock and of acute respiratory distress syndrome.

22. The use of compounds of the formula I as claimed in claim 8 for producing drugs for the treatment of immunological disorders such as inflammations and rheumatic disorders such as, for example, rheumatoid arthritis.

23. The use of compounds of the formula I as claimed in claim 8 for producing drugs for the treatment of diabetes mellitus.

24. A compound of the formula III

CLAIMS - OZ 50761



III

in which

A is a C_1-C_3 chain it being possible for each carbon atom also to carry one or two of the following substituents: C_1-C_4-alkyl, OH, O-C_1-C_4-alkyl, CO_2H, Co_2.C_1-C_4-alkyl and phenyl or one C atom may also carry an =O group, and

X^1 and R^1 have the meanings stated in claim 1,

excluding the compounds

9-amino-3-methyl-1,2,3,4-tetrahydro-5H-1,4-benzodiazepin-5-one,

9-amino-3-methyl-3,4-dihydro-1H-1,4-benzodiazepine-2,5-dione,

6,8-diamino-2,4-(1H,3H)-quinazolinedione,

8-amino-2,4-(1H,3H)-quinazolinedione,

and the salts thereof.

25. A process for preparing compounds of the formula III and salts thereof, wherein 2-halo-3-nitrobenzoic esters are reacted with a suitable diamine in a polar solvent in the presence of a base, and then the nitro group is hydrogenated with hydrogen in the presence of a suitable catalyst.

26. The use of compounds of the formula III in the synthesis of PARP inhibitors.

Benzodiazepine derivatives, the preparation and use thereof

The present invention relates to novel benzodiazepine derivatives, their preparation and the use as inhibitors of the enzyme poly(ADP-ribose) polymerase or PARP (EC 2.4.2.30) for producing drugs.

Poly(ADP-ribose) polymerase (PARP) or, as it is also called, poly(ADP-ribose) synthase (PARS) is a regulatory enzyme which is found in cell nuclei (K. Ikai et al., J. Histochem. Cytochem. 1983, 31, 1261-1264). It is assumed that PARP is involved in the repair of DNA breaks (M.S. Satoh et al., Nature 1992, 356, 356-358). Damage or breaks in DNA strands activate the enzyme PARP which, when it is activated, catalyzes the transfer of ADP-ribose from NAD (S. Shaw, Adv. Radiat. Biol., 1984, 11, 1-69). During this, nicotinamide is released from NAD. Nicotinamide is converted back into NAD by other enzymes with consumption of the energy carrier ATP. Overactivation of PARP would accordingly result in nonphysiologically large consumption of ATP, and this leads in the extreme case to cell damage and cell death.

It is known that free radicals such as superoxide anion, NO and hydrogen peroxide may lead to DNA damage in cells and thus activate PARP. The formation of large amounts of free radicals is observed in a number of pathophysiological states, and it is assumed that this accumulation of free radicals leads or contributes to the observed cell or organ damage. This includes, for example, ischemic states of organs as in stroke, myocardial infarct (C. Thiemermann et al., Proc. Natl. Acad. Sci. USA, 1997, 94, 679-683) or ischemia of the kidneys, but also reperfusion damage as occurs, for example, after lysis of myocardial infarct (see above: C. Thiemermann et al.). Inhibition of the enzyme PARP might accordingly be a means of at least partly preventing or moderating this damage. PARP inhibitors might thus represent a novel therapeutic principle for treating a number of diseases.

The enzyme PARP influences the repair of DNA damage and might thus also play a part in the therapy of cancers, since a greater action potential on tumor tissue was observed (G. Chen et al. Cancer Chemo. Pharmacol. 1988, 22, 303) in combination with substances with cytostatic activity.

Nonlimiting examples of tumors are leukemia, glioblastomas, lymphomas, melanomas, and carcinomas of the breast and cervix.

It has additionally been found that PARP inhibitors may show an immunosuppressant effect (D. Weltin et al. *Int. J. Immunopharmacol.* 1995, 17, 265-271).

It has likewise been discovered that PARP is involved in immunological disorders or diseases in which the immune system plays an important part, such as, for example, rheumatoid arthritis and septic shock, and that PARP inhibitors may show a beneficial effect on the course of the disease (H. Kröger et al. *Inflammation* 1996, 20, 203-215; W. Ehrlich et al. *Rheumatol. Int.* 1995, 15, 171-172; C. Szabo et al., *Proc. Natl. Acad. Sci. USA* 1998, 95, 3867-3872; S. Cuzzocrea et al. *Eur. J. Pharmacol.* 1998, 342, 67-76).

PARP means for the purpose of this invention also isoenzymes of the PARP enzyme described above.

In addition, the PARP inhibitor 3-aminobenzamide showed protective effects in a model of circulatory failure (S. Cuzzocrea et al., *Br. J. Pharmacol.* 1997, 121, 1065-1074). There is likewise experimental evidence that inhibitors of the enzyme PARP might be of benefit as agents for treating diabetes mellitus (V. Burkart et al. *Nature Med.* 1999, 5, 314-319).

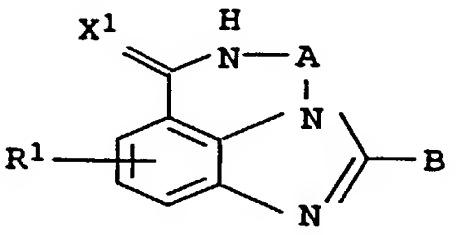
Benzodiazepines and benzodiazepinones and their derivatives represent a class of chemicals which have been widely used in organic synthesis. Derivatives of these compounds additionally having a fused-on imidazo ring, that is to say imidazobenzodiazepinones, have scarcely been described, however. Aminodibenzodiazepinones were prepared in P.V. Khadikar et al. J. Heterocycl. Chem. 1998, 35, 675. Thus, simple derivatives having radicals such as chlorine or nitro on the benzo ring and a methyl group on the imidazo ring were prepared in Geneste et al., Eur. J. Chem. Chim. Ther. 1978, 13, 53. In M.J. Kukla et al., J. Med. Chem. 1991, 34, 3187, a dihydroimidazobenzodiazepinone was prepared as intermediate for active substances said to have an anti-HIV effect.

The compounds of the general formula I according to this invention have not previously been described and are accordingly novel.

It has additionally been found, surprisingly, that benzodiazepine derivatives having a fused-on ring are very effective inhibitors of the enzyme PARP.

The present invention describes novel benzodiazepine derivatives of the general formula I which are potent PARP inhibitors.

The present invention relates to substituted benzodiazepine derivatives of the general formula I



I

in which

A can be a C_1-C_3 chain where each carbon atom may also carry one or two of the following substituents: C_1-C_4-alkyl, OH, O-C_1-C_4-alkyl, COOH, COO-C_1-C_4-alkyl and phenyl or one C atom may also carry an =O group, and

X^1 can be S, O and NH, and

R^1 is hydrogen, chlorine, fluorine, bromine, iodine, branched and unbranched C_1-C_6-alkyl, OH, nitro, CF_3, CN, $NR^{11}R^{12}$, NH-CO-R^{13}, O-C_1-C_4-alkyl, where R^{11} and R^{12} are, independently of one another, hydrogen or C_1-C_4-alkyl, and R^{13} is hydrogen, C_1-C_4-alkyl, C_1-C_4-alkyl-phenyl or phenyl, and

B can be an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 15 carbon atoms, an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 14 carbon atoms and 0 to 5 nitrogen atoms, 0 to 2 oxygen atoms or 0 to 2 sulfur atoms, each of which may also be substituted by one R^4 and a maximum of 3 different or identical R^5 radicals, and one or two carbon or sulfur atoms may also carry one or two =O groups, such as, for example, keto groups, sulfones or sulfoxides, or is a radical L_v-Y-M_w in which

L can be a straight-chain or branched, saturated or unsaturated carbon chain of 1 to 8 C atoms, it being possible for each carbon atom to be substituted by one or two R^4 radicals and a maximum of two different or identical R^5 radicals, and

M has, independently of L, the same meaning as L, and

Y is a bond, or can be S, O or NR^3, where R^3 can be hydrogen, branched and unbranched C_1-C_6-alkyl, C_1-C_4-alkyl-phenyl, phenyl, and

v can be 0 and 1, and

w can be 0 and 1, and

when Y is a bond, R^4 and R^5 are not both hydrogen, and

when B is L_v-Y-M_w, R^1 is not chlorine or NO_2, and

R^4 is hydrogen and $-(D)_p-(E)_s-(F^1)_q-G^1-(F^2)_r-(G^2)-G^3$, where

D can be S, NR^{43} and O

E can be phenyl,

>C=O, $-SO_2-$, $-SO_2NH-$, $-NHCO-$, $-CONH-$, $NHSO_2-$, $-NHCOCH_2X^4$,

and

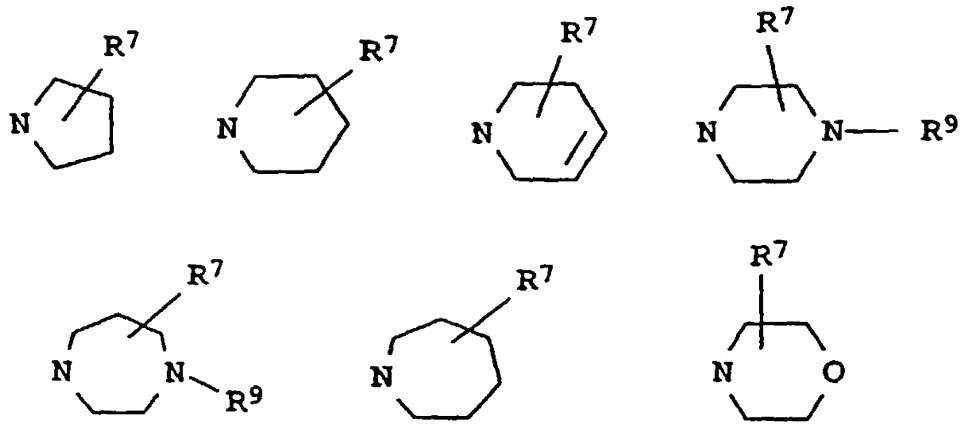
X^4 can be S, O or NH, and

F^1 can be a straight-chain or branched saturated or unsaturated carbon chain of 1 to 8 C atoms, and

F^2 has, independently of F^1, the same meaning as F^1,

G^1 is a bond or can be an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 15 carbon atoms, an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 14 carbon atoms and 0 to 5 nitrogen atoms, 0 to 2 oxygen atoms or 0 to 2 sulfur atoms, each of which may also be substituted by a maximum of 3 different or identical R^5 radicals, and one or two carbon or sulfur atoms may also carry one or two =O groups, and

G^2 is $NR^{41}R^{42}$ and



or a bond, and

G^3 can be an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 15 carbon atoms, an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 14 carbon atoms and 0 to 5 nitrogen atoms, 0 to 2 oxygen atoms or 0 to 2 sulfur atoms, each of which may also be substituted by a maximum of 3 different or identical radicals R^5, and one or two carbon or sulfur atoms may also carry one or two =O groups, or is hydrogen, and

p can be 0 and 1 and

s can be 0 and 1 and

q can be 0 and 1 and

r can be 0 and 1 and

R^{41} can be hydrogen, C_1-C_6-alkyl, it being possible for each carbon atom also to carry up to two R^6 radicals, phenyl which may also carry a maximum of two R^6 radicals, and $(CH_2)_t$-K and

R^{42} can be hydrogen, C_1-C_6-alkyl, -CO-R^8, CO_2-R^8, SO_2NH_2, SO_2-R_8, -(C=NH)-R^8 and -(C=NH)-NHR^8 and

R^{43} can be hydrogen and C_1-C_4-alkyl and

t can be 1, 2, 3, 4 and

K can be $NR^{11}R^{12}$, NR^{11}-C_1-C_4-alkyl-phenyl, pyrrolidine, piperidine, 1,2,5,6-tetrahydropyridine, morpholine, homopiperidine, piperazine, which may also be substituted by

an alkyl radical C_1-C_6-alkyl, and homopiperazine which may also be substituted by an alkyl radical C_1-C_6-alkyl, and

R^5 can be hydrogen, chlorine, fluorine, bromine, iodine, OH, nitro, CF_3, CN, $NR^{11}R^{12}$, NH-CO-R^{13}, C_1-C_4-alkyl-CO-NH-R^{13}, COR^8, C_0-C_4-alkyl-O-CO-R^{13}, C_1-C_4-alkyl-phenyl, phenyl, CO_2-C_1-C_4-alkyl, and branched and unbranched C_1-C_6-alkyl, O-C_1-C_4-alkyl, S-C_1-C_4-alkyl, it being possible for each C atom of the alkyl chains to carry up to two R^6 radicals, and for the alkyl chains also to be unsaturated, and

R^6 can be hydrogen, chlorine, fluorine, bromine, iodine, branched and unbranched C_1-C_6-alkyl, OH, nitro, CF_3, CN, $NR^{11}R^{12}$, NH-CO-R^{13}, O-C_1-C_4-alkyl,

R^7 can be hydrogen, C_1-C_6-alkyl, phenyl, it being possible for the ring also to be substituted by up to two R^{71} radicals, and an amine $NR^{11}R^{12}$ or a cyclic saturated amine which has 3 to 7 members, and may also be substituted by an alkyl radical C_1-C_6-alkyl, and homopiperazine which may also be substituted by an alkyl radical C_1-C_6-alkyl,

and where the radicals R^{11}, R^{12} and R^{13} in K, R^5, R^6 and R^7 may, independently of one another, assume the same meaning as for R^1, and

R^{71} can be OH, C_1-C_6-alkyl, O-C_1-C_4-alkyl, chlorine, bromine, iodine, fluorine, CF_3, nitro, NH_2, and

R^8 can be C_1-C_6-alkyl, CF_3, phenyl, C_1-C_4-alkyl-phenyl, it being possible for the ring also to be substituted by up to two R^{81} radicals, and

R^{81} can be OH, C_1-C_6-alkyl, O-C_1-C_4-alkyl, chlorine, bromine, iodine, fluorine, CF_3, nitro, NH_2, and

R^9 can be hydrogen, C_1-C_6-alkyl, C_1-C_4-alkyl-phenyl, CO_2-C_1-C_4-alkyl-phenyl, CO_2-C_1-C_4-alkyl, SO_2-phenyl, COR_8 and phenyl, it being possible for the phenyl rings also to be substituted by up to two R^{91} radicals, and

R^{91} can be OH, C_1-C_6-alkyl, O-C_1-C_4-alkyl, chlorine, bromine, iodine, fluorine, CF_3, nitro, NH_2,

and their tautomeric forms, possible enantiomeric and diastereomeric forms, and prodrugs thereof.

Preferred compounds of the formula I are those where

A is a C_2 chain, which may be substituted, and

X^1 is O, and

R^1 is hydrogen.

Preferred compounds of the formula I are those as indicated above, in which

B can be an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 15 carbon atoms, an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 14 carbon atoms and 0 to 5 nitrogen atoms, 0 to 2 oxygen atoms or 0 to 2 sulfur atoms, each of which may also be substituted by one R^4 and a maximum of 3 different or identical R^5 radicals, and one or two carbon or sulfur atoms may also carry one or two =O groups.

Particularly preferred radicals for B are:

B phenyl, cyclohexyl, piperidine, pyridine, pyrimidine, pyrrole, pyrazole, thiophene, furan, oxazole, naphthalene, piperazine, quinoline, pyrazine, which may also be substituted by one R^4 or a maximum of 2 R^5.

Very particularly preferred compounds of the formula I are those where

R^4 is hydrogen or $D_{0,1}$-$F^1{}_{0,1}$-G^2-G^3 with G^3 equal to hydrogen and

D is O and NR^{43}, where R^{43} is hydrogen and C_1-C_3-alkyl and

F^1 is C_2-C_4-alkyl.

Additional particularly preferred compounds of the formula I are those where B is L_v-Y-M_w where

v is 0, and

w is 1, and

Y is a bond, and

M can be a straight-chain or branched carbon chain of 2 to 8 C atoms, which contains at least one double bond, it being possible for each carbon atom to be substituted by one or two R^4 radicals and a maximum of two different or identical R^5 radicals, and

R^1 is hydrogen, and

R^4 is $D_{0,1}$-$F^1{}_{0,1}$-G^1-G^2-G^3 with G^3 equal to hydrogen, and

D is O and NR^{43}, where R^{43} is hydrogen and C_1-C_3-alkyl and

F^1 is C_2-C_4-alkyl.

The use of compounds of the general formula I for producing medicines with a PARP-inhibiting effect is likewise claimed, with R^1, X^1 and A having the same meaning as above, and it being possible for B to be hydrogen and a C_1-C_6 alkyl chain.

The compounds of the formula I can be employed as racemates, as enantiomerically pure compounds or as diastereomers. If enantiomerically pure compounds are required, they can be obtained, for example, by carrying out a conventional racemate resolution with the compounds of the formula I or their intermediates using a suitable optically active base or acid.

Alkyl chains may in each case be branched or unbranched. Unbranched alkyl chains are preferred.

The invention thus also relates to compounds which are mesomers or tautomers of compounds of the formula I.

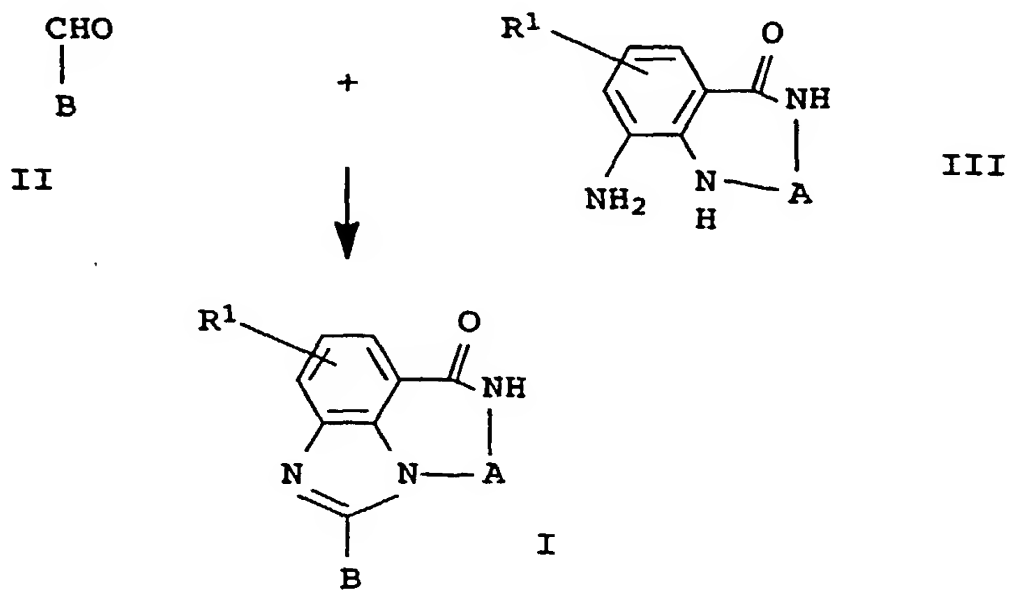
The invention further relates to the physiologically tolerated salts of the compounds I, which can be obtained by reacting compounds I with a suitable acid or base. Suitable acids and bases are listed, for example, in Fortschritte der Arzneimittelforschung, 1966, Birkhäuser Verlag, volume 10, pages 224-285. These include, for example, hydrochloric acid, citric acid, tartaric acid, lactic acid, phosphoric acid, methanesulfonic acid, acetic acid, formic acid, maleic acid, fumaric acid etc., and sodium hydroxide, lithium hydroxide, potassium hydroxide and tris.

Prodrugs mean compounds which are metabolized in vivo to compounds of the general formula I. Typical prodrugs are phosphates, carbamates of amino acids, esters and others.

The benzodiazepine derivatives I according to the invention can be prepared in various ways, as outlined in synthesis schemes 1-3.

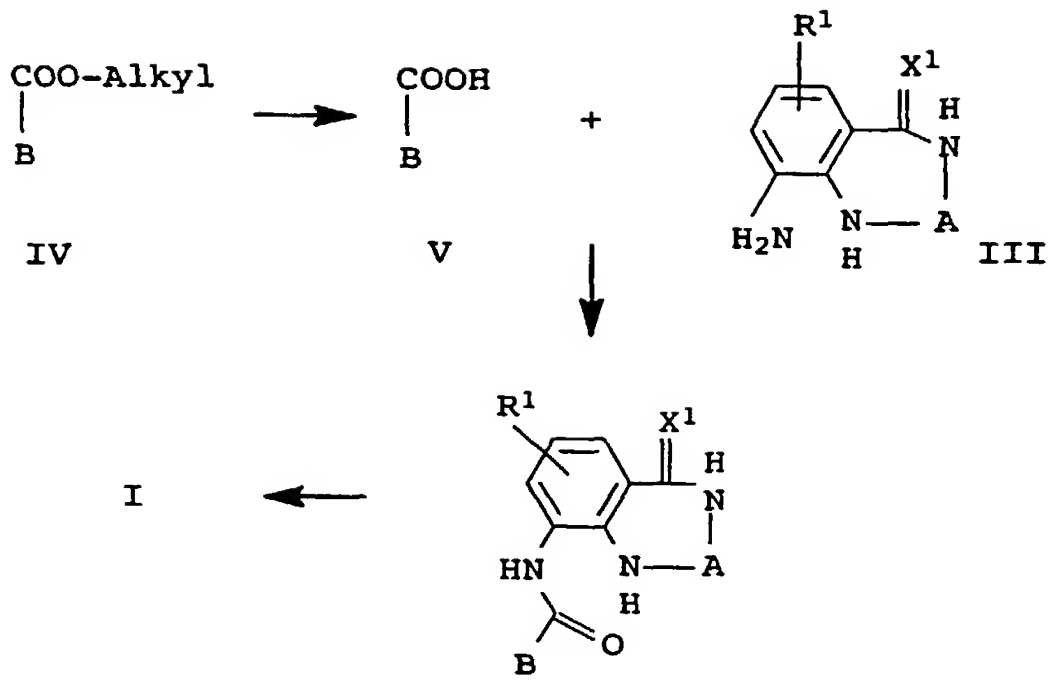
The possible methods of synthesis are essentially already known or are based on analogous routes which are known.

Synthesis scheme 1



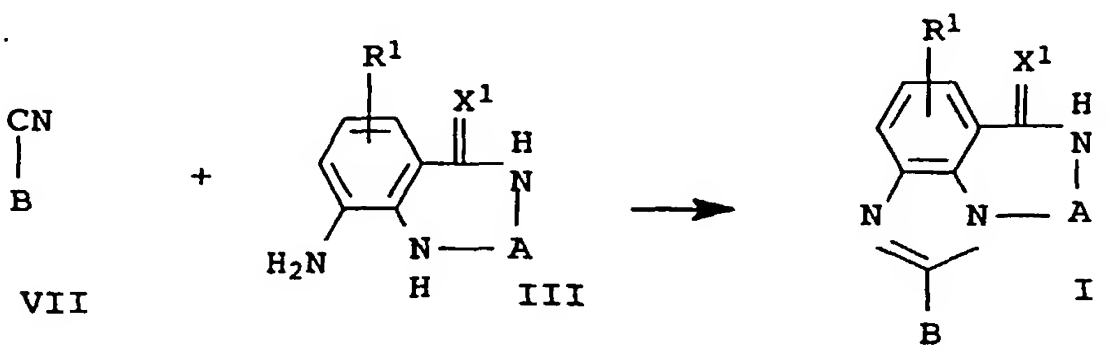
Condensation of the aldehyde II with diamines III results in the benzimidazole I, this preferably being done in polar solvents such as ethanol or dimethylformamide with addition of acids such as acetic acid at elevated temperature, ordinarily 80-120°C. It is beneficial for the reaction to add weak oxidizing agents such as, for example, copper(II) salts which are added, for example, as aqueous solutions.

Scheme 2



As an alternative to the aldehydes II shown in scheme I, it is also possible to employ acids such as V (see scheme 2) or nitriles such as VII (see scheme 3) in place of the aldehyde. Reaction of these derivatives takes place in analogy to the preparation from the substituted aldehydes II. Starting from V the condensation to II takes place in two stages. Firstly, the acid V is reacted with the aniline III in a peptide-like coupling to give the amide VI. This is carried out under conventional conditions which are listed, for example, in Houben-Weyl, Methoden der Organischen Chemie, 4th Edition, E5, chapter V, and R.C. Larock, Comprehensive Organic Transformations, VCH Publisher, 1989, pages 972 et seq. The ring closure to the benzimidazole then takes place at elevated temperature, for example 60 to 180°C, with or without solvents such as dimethylformamide, with the addition of acids such as acetic acid or directly in acetic acid itself.

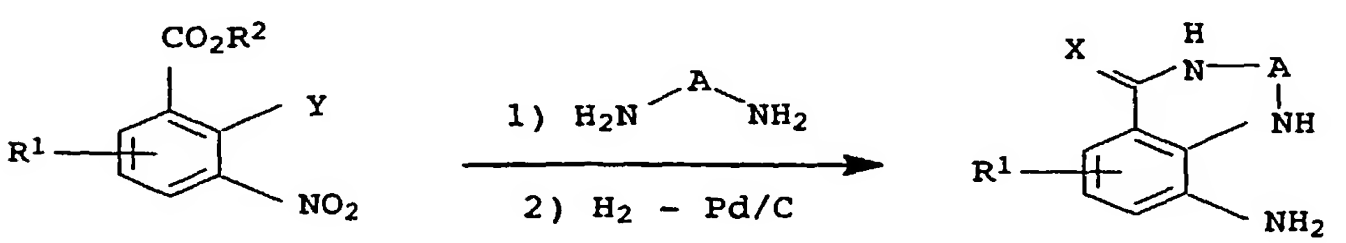
Scheme 3



Reaction of the diamine III with a nitrile VII likewise takes place under conventional conditions. This may entail the use of solvents such as dimethylformamide with the addition of acids or else the use of polyphosphoric acid at elevated temperature such as 60 to 200°C. It is, however, also possible to use the conventional methods for preparing amidines from benzonitriles as described in Houben-Weyl, Methoden der organischen Chemie, E5, pages 1304 et seq., J. Amer. Chem. Soc. 1957, 427 and J. Org. Chem. 1987, 1017.

Compounds III are synthesized as shown in scheme 4 by reacting a substituted nitrobenzoic ester IX with a suitable diamine in a polar solvent such as dimethylformamide in the presence of a base such as potassium carbonate at 100°C to 150°C, preferably at 110°C to 130°C, in particular at about 120°C, followed by hydrogenation in the presence of a suitable catalyst such as 10% palladium on carbon.

Scheme 4

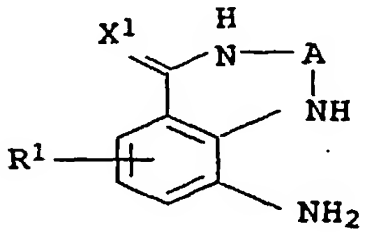


IX

Y = Halogen

III

The invention additionally relates to the intermediates of the formula III



III

in which

A is a C_1-C_3 chain it being possible for each carbon atom also to carry one or two of the following substituents: C_1-C_4-alkyl, OH, O-C_1-C_4-alkyl, CO_2H, CO_2-C_1-C_4-alkyl and phenyl or one C atom may also carry an =O group, and

X^1 and R^1 have the meanings stated previously,

excluding the compounds
9-amino-3-methyl-1,2,3,4-tetrahydro-5H-1,4-benzodiazepin-5-one,
9-amino-3-methyl-3,4-dihydro-1H-1,4-benzodiazepine-2,5-dione,
6,8-diamino-2,4-(1H,3H)-quinazolinedione,
8-amino-2,4-(1H,3H)-quinazolinedione
and the salts thereof.

Additionally a process for preparing compounds of the formula III and their salts, where 2-halo-3-nitrobenzoic esters are reacted with a suitable diamine in a polar solvent in the presence of a base, and then the nitro group is hydrogenated with hydrogen in the presence of a suitable catalyst,

and the use of compounds of the formula III in the synthesis of PARP inhibitors.

The substituted benzodiazepine derivatives I contained in the present invention are inhibitors of the enzyme poly(ADP-ribose) polymerase or PARP (EC 2.4.2.30).

The inhibitory effect of the substituted benzodiazepine derivatives I can be determined using an enzyme assay which has already been disclosed in the literature, with a K_i being determined as a gauge of the effect. The benzodiazepine derivatives I were measured in this way for an inhibitory effect on the enzyme poly(ADP-ribose) polymerase or PARP (EC 2.4.2.30).

The substituted benzodiazepine derivatives of the general formula I are inhibitors of poly(ADP-ribose) polymerase (PARP) or, as it is also called, poly(ADP-ribose) synthase (PARS) and can thus be used for the treatment and prophylaxis of diseases associated with an increased activity of these enzymes.

The compounds of the formula I can be employed to produce drugs for treating damage following ischemias and for the prophylaxis of expected ischemias in various organs.

The present benzodiazepine derivatives of the general formula I can accordingly be used for the treatment and prophylaxis of neurodegenerative disorders occurring after ischemia, trauma (craniocerebral trauma), massive bleeding, subarachnoid hemorrages and stroke, and of neurodegenerative disorders such as multi-infarct dementia, Alzheimer's disease, Huntington's disease and of epilepsies, in particular of generalized epileptic seizures such as, for example, petit mal and tonoclonic seizures

and partial epileptic seizures such as temporal lobe, and complex partial seizures, and further for the treatment and prophylaxis of damage to the heart after cardiac ischemias and damage to the kidneys after renal ischemias, for example of acute renal insufficiency caused by drug therapies such as, for example, associated with cyclosporin treatment, of acute kidney failure or of damage occurring during and after a kidney transplant. The compounds of the general formula I can further be used for treatment of acute myocardial infarct and damage occurring during and after medical lysis thereof (for example with TPA, reteplase, streptokinase or mechanically with a laser or Rotablator) and of microinfarcts during and after heart valve replacement, aneurysm resections and heart transplants. The present benzodiazepine derivatives I can likewise be used for treatment in cases of revascularization of critically narrowed coronary arteries, for example in PTCA and bypass operations, and critically narrowed peripheral arteries, for example leg arteries. In addition, the benzodiazepine derivatives I can be beneficial in the treatment of tumors and metastasis thereof, and be used for treating inflammations and rheumatic disorders such as, for example, rheumatoid arthritis, and for the treatment of diabetes mellitus, for the treatment of multiorgan failure, for example associated with septic shock, and for the treatment of ARDS ("acute respiratory distress syndrome", shock lung).

The pharmaceutical preparations according to the invention contain a therapeutically effective amount of the compounds I in addition to conventional pharmaceutical excipients.

For local external use, for example, in dusting powders, ointments or sprays, the active substances can be present in the usual concentrations. The active substances are ordinarily present in an amount of 0.001 to 1% by weight, preferably 0.001 to 0.1% by weight.

For internal use, the preparations are administered in single doses. From 0.1 to 100 mg are given per kg of body weight in a single dose. The preparation may be administered in one or more doses each day, depending on the nature and severity of the disorders.

Appropriate for the required mode of administration, the pharmaceutical preparations according to the invention comprise conventional carriers and diluents, in addition to the active substance. For local external use, it is possible to use pharmaceutical excipients such as ethanol, isopropanol, ethoxylated castor oil, ethoxylated hydrogenated castor oil,

polyacrylic acid, polyethylene glycol, polyethylene glycol stearate, ethoxylated fatty alcohols, liquid paraffin, petrolatum and wool fat. Examples suitable for internal use are lactose, propylene glycol, ethanol, starch, talc and polyvinylpyrrolidone.

It is also possible for antioxidants such as tocopherol and butylated hydroxyanisole, and butylated hydroxytoluene, flavor-improving additives, stabilizers, emulsifiers and lubricants to be present.

The substances present in the preparation in addition to the active substance, and the substances used in the production of the pharmaceutical preparations are toxicologically acceptable and compatible with the particular active substance. The pharmaceutical preparations are produced in a conventional way, for example by mixing the active substance with conventional carriers and diluents.

The pharmaceutical preparations can be administered in various ways, for example orally, parenterally such as intravenously by infusion, subcutaneously, intraperitoneally and topically. Thus, possible presentations are tablets, emulsions, infusion and injection solutions, pastes, ointments, gels, cremes, lotions, dusting powders and sprays.

Pharmacological example:
Inhibition of the enzyme poly(ADP-ribose) polymerase or PARP (EC 2.4.2.30)

A 96-well microtiter plate (Falcon) is coated with histones (type II-AS; SIGMA H7755). For this purpose, histones are dissolved in a concentration of 50 µg/ml in carbonate buffer (0.05 M $NaHCO_3$; pH 9.4). The individual wells of the microtiter plates are each incubated with 100 µl of this histone solution overnight. The histone solution is then removed, and the individual wells are incubated with 200 µl of a 1% strength BSA (bovine serum albumin) solution in carbonate buffer at room temperature for 2 hours. This is followed by washing three times with washing buffer (0.05% Tween10 in PBS). For the enzyme reaction, 50 µl of the enzyme reaction solution (5 µl of reaction buffer (1 M tris-HCl pH 8.0, 100 mM $MgCl_2$, 10 mM DTT), 0.5 µl of PARP (c = 0.22 µg/µl), 4 µl of activated DNA (SIGMA D-4522, 1 mg/ml in water), 40.5 µl of H_2O) are preincubated in each well with 10 µl of an inhibitor solution for 10 minutes. The enzyme reaction is started by adding 40 µl of a substrate solution (4 µl of reaction buffer (see above), 8 µl of NAD solution (100 µM in H_2O), 28 µl of H_2O). The reaction time is 20 minutes at room temperature. The reaction is

stopped by washing three times with washing buffer (see above). This is followed by incubation at room temperature with a specific anti-poly(ADP-ribose) antibody for one hour. The antibodies used were "10H" monoclonal anti-poly(ADP-ribose) antibodies (Kawamaitsu H et al. (1984) Monoclonal antibodies to poly(adenosine diphosphate ribose) recognize different structures. Biochemistry 23, 3771-3777). It is likewise possible to use polyclonal antibodies.

The antibodies were employed in a 1:5000 dilution in antibody buffer (1% BSA in PBS; 0.05% Tween20). Washing three times with washing buffer is followed by incubation at room temperature with the secondary antibody for one hour. In this case the monoclonal antibody used was an anti-mouse IgG coupled to peroxidase (Boehringer Mannheim), and the rabbit antibody was an anti-rabbit IgG coupled to peroxidase (SIGMA A-6154), each in a 1:10,000 dilution in antibody buffer. After washing three times with washing buffer, the color reaction is carried out using 100 µl/well color reagent (SIGMA, TMB mixture, T8540) at room temperature for about 15 min. The color reaction is stopped by adding 100 µl of 2 M H_2SO_4. Measurement is carried out immediately thereafter (450 nm versus 620 nm; "Easy Reader" EAR340AT ELISA plate reader, SLT-Labinstruments, Austria). The IC50 of an inhibitor to be measured is the concentration of inhibitor at which a half-maximum change in color concentration occurs.

Examples

Example 1

2-(4-(4-Methylpiperazin-1-yl)phenyl)-5,6-dihydroimidazo-[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

a) 9-Nitro-1,2,3,4-tetrahydro-5H-1,4-benzodiazepin-5-one
24 g (0.11 mol) of methyl 2-chloro-3-nitrobenzoate were dissolved in 250 ml of dimethylformamide. 15.4 g (0.11 mol) of potassium carbonate and 22.3 ml (0.33 mol) of ethylenediamine were successively added, and the mixture was heated at 120°C for 3 hours. The mixture was then concentrated to half the volume in vacuo, and the residue was poured into water, whereupon the product precipitated. 19.7 g of the product were obtained.

b) 9-Amino-1,2,3,4-tetrahydro-5H-1,4-benzodiazepin-5-one
1.7 g of 10% palladium/carbon were added to 19 g (91.7 mmol) of the intermediate 1a in 500 ml of ethanol, and it was then hydrogenated with hydrogen. The mixture was then filtered.

The filtrate was concentrated in vacuo, and the residue was recrystallized from isopropanol/ether. The crystals which separated out were filtered off with suction. 14.4 g of the product were obtained.

c) 2-(4-(4-Methylpiperazin-1-yl)phenyl)-5,6-dihydroimidazo-[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

2.0 g (11.3 mmol) of the intermediate 1b and 2.8 ml (45.15 mmol) of concentrated acetic acid were dissolved in 200 ml of methanol and, at room temperature, a solution of 3.0 g (14.7 mmol) of 4-(4-methylpiperazin-1-yl)benzaldehyde in 50 ml of methanol was added dropwise. The mixture was stirred at room temperature for 1 hour. Then 2.9 g (14.7 mmol) of copper(II) acetate dissolved in 100 ml of water were added dropwise, and the mixture was refluxed for 30 minutes. During this time, in parallel a solution of 4.1 g (17 mmol) of sodium sulfide x 9 H_20 in 70 ml of water and a solution of 17 ml of 1 M hydrochloric acid in 50 ml of water were added. After cooling, the resulting precipitate was filtered off with suction, and the filtrate was concentrated in vacuo. The resulting residue was partitioned between aqueous sodium bicarbonate solution and ethyl acetate. The organic phase was separated off, dried and concentrated in vacuo. The residue was crystallized from ethyl acetate/ether. 2.4 g of the product were obtained.

^{1}H-NMR (D_6-DMSO): δ = 2.2 (3H), 2.5 (4H), 3.3 (4H), 3.5 (2H), 4.4 (2H), 7.1 (2H), 7.3 (1H), 7.7-7.9 (4H) and 8.4 (1H) ppm.
[M^+ = 361]

Example 2

2-(4-Nitrophenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

The product was obtained in analogy to the method in 1c from 9-amino-1,2,3,4-tetrahydro-5H-1,4-benzodiazepin-5-one and 4-nitrobenzaldehyde.

^{1}H-NMR (D_6-DMSO): δ = 3.6 (2H), 4.5 (2H), 7.4 (1H) and 7.9-8.6 (7H) ppm.
[M^+ = 308]

Example 3

2-(4-(2-N,N-Diethylaminoeth-1-yloxy)phenyl)-5,6-dihydroimidazo-[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

The product was obtained in analogy to the method in 1c from 9-amino-1,2,3,4-tetrahydro-5H-1,4-benzodiazepin-5-one and 4-(2-N,N-diethylaminoeth-1-yloxy)benzaldehyde.

^{1}H-NMR (D_6-DMSO): δ = 1.0 (6H), 2.6 (4H), 2.8 (1H), 3.5 (2H), 4.1 (2H), 4.5 (2H), 7.1 (2H), 7.4 (1H), 7.7-7.9 (4H) and 8.4 (1H) ppm.
[M^+ = 378]

The following further examples were prepared in analogy to the above methods:

Example 4

2-(4-(2-Piperidin-1-yleth-1-yloxy)phenyl)-5,6-dihydroimidazo-[4,5,1-jk]-[1,4]benzodiazepin-7(4H)-one

The product was obtained in analogy to the method in 1c from 9-amino-1,2,3,4-tetrahydro-5H-1,4-benzodiazepin-5-one and 4-(2-piperidin-1-yleth-1-yloxy)benzaldehyde.

^{1}H-NMR (D_6-DMSO): δ = 1.3-1.6 (6H), 2.5 (4H), 2.7 (2H), 3.6 (2H), 4.2 (2H), 4.5 (2H), 7.1 (2H), 7.4 (1H), 7.7-7.9 (4H) and 8.4 (1H) ppm.
[M^+ = 390]

Example 5

2-(4-(N-(2-N,N-Diethylaminoeth-1-yl)-N-methylamino)phenyl)-5,6-dihydroimidazo[4,5,1-jk]-[1,4]benzodiazepin-7(4H)-one

The product was obtained in analogy to the method in 1c from 9-amino-1,2,3,4-tetrahydro-5H-1,4-benzodiazepin-5-one and 4(N-(2-N,N-diethylaminoeth-1-yl)-N-methylamino)benzaldehyde.

^{1}H-NMR (D_6-DMSO): δ = 0.9 (6H), 2.5 (6H), 3.0 (3H), 3.4-3.6 (4H), 4.45 (2H), 6.8 (2H), 7.3 (1H), 7.6-7.9 (4H) and 8.45 (1H) ppm.
[M^+ = 391]

Example 6

2-(4-(4-(tert-Butyloxycarbonyl)piperazin-1-yl)phenyl)-5,6-dihydroimidazo[4,5,1-jk]-[1,4]benzodiazepin-7(4H)-one

The product was obtained in analogy to the method in 1c from 9-amino-1,2,3,4-tetrahydro-5H-1,4-benzodiazepin-5-one and 4-(4-(tert-butyloxycarbonyl)piperazin-1-yl)benzaldehyde.

^{1}H-NMR (D_6-DMSO): δ = 1.4 (9H), 3.3 (4H), 3.4-3.6 (6H), 4.45 (2H), 7.1 (2H), 7.3 (1H), 7.7-7.9 (4H) and 8.4 (1H) ppm.
[M^+ = 447]

Example 7

2-(4-(4(tert-Butyloxycarbonyl)homopiperazin-1-yl)phenyl)-5,6-dihydroimidazo[4,5,1-jk]-[1,4]benzodiazepin-7(4H)-one

The product was obtained in analogy to the method in 1c from 9-amino-1,2,3,4-tetrahydro-5H-1,4-benzodiazepin-5-one and 4-(4-(tert-butyloxycarbonyl)homopiperazin-1-yl)benzaldehyde.

^{1}H-NMR (D_6-DMSO): δ = 1.2-1.3 (9H), 1.8-1.9 (2H), 3.2-3.8 (10H), 4.45 (2H), 6.9 (2H), 7.3 (1H), 7.7 (2H), 7.8 (2H) and 8.4 (1H) ppm.
[M^+ = 461]

Example 8

2-(4-(Homopiperazin-1-yl)phenyl)-5,6-dihydroimidazo[4,5,1-jk]-[1,4]benzodiazepin-7(4H)-one

The product was prepared from the product from Example 7 in analogy to Example 9.
[M^+ = 361]

Example 9

2-(4-(Piperazin-1-yl)phenyl-5,6- dihydroimidazo[4,5,1-jk]-[1,4]benzodiazepin-7(4H)-one trihydrochloride

0.5 g of Example 6 was added to 30 ml of isopropanolic hydrogen chloride solution at room temperature and stirred for several hours. The mixture was then concentrated in vacuo, and the resulting residue was recrystallized from ethanol. The product was obtained as trihydrochloride.

^{1}H-NMR (D_6-DMSO): δ = 3.2-3.8 (10H), 4.5 (2H), 7.2 (2H), 7.5-8.0 (5H), 8.6 (1H) and 9.6 (broad) ppm.
[M^+ = 347]

Example 10
2-(4-Aminophenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one × 2 HCl
[M^+ = 280]

Example 11
2-(Piperidin-4-yl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one × HCl
[M^+ = 271]

Example 12
2-(1-n-Propylpiperidin-4-yl)-5,6-dihydroimidazo[4,5,1-*jk*]-[1,4]benzodiazepin-7(4*H*)-one × HCl
[M^+ = 313]

Example 13
2-(1-Benzylpiperidin-4-yl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]-benzodiazepin-7(4*H*)-one × HCl
[M^+ = 361]

Example 14
2-(Pyridin-4-yl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one × HCl
[M^+ = 265]

Example 15
2-(Thien-3-yl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one × HCl
[M^+ = 270]

Example 16
2-(Quinolin-3-yl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one × HCl
[M^+ = 315]

Example 17
2-(Naphth-2-yl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+ = 313]

Example 18
2-(1*H*-Imidazol-1-yl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one × HCl

[M^+ = 330]

Example 19

2-(4-(3-Formylpyrrol-1-yl)phenyl)-5,6-dihydroimidazo[4,5,1-*jk*]-[1,4]benzodiazepin-7(4*H*)-one

[M^+ = 356]

Example 20

2-(4-(3-Trifluoroacetamidomethylpyrrol-1-yl)phenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one × HCl

[M^+ = 453]

Example 21

2-(4-(4-(Piperidin-1-yl)piperidin-1-yl)phenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one × 2 HCl

[M^+ = 432]

Example 22

2-(4-(3-(Piperidin-1-ylmethyl)pyrrol-1-yl)phenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one × HCl

[M^+ = 427]

Example 23

2-(4-(3-Aminomethylpyrrol-1-yl)phenyl)-5,6-dihydroimidazo-[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one × HCl

[M^+ = 358]

Example 24

2-(3-(2-(N,N-Dimethylamino)eth-1-yl)-4-nitrophenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one × HCl

[M^+ = 380]

Example 25

5,6-Dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one

[M^+ = 187]

Example 26

2-(Pyrazin-2-yl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one × HCl

[M^+ = 266]

Example 27

2-(2-(tert-Butyloxycarbonylaminomethyl)thiazol-4-yl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one

[M^+ = 399]

Example 28
2-(2-(Aminomethyl)thiazol-4-yl)-5,6-dihydroimidazo[4,5,1-*jk*]-[1,4]benzodiazepin-7(4*H*)-one × HCl
[M^+ = 300]

Example 29
2-(2-fluoro-4-(pyridin-4-yl)phenyl)-5,6-dihydroimidazo-[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+ = 358]

Example 30
2-(1-(1-Methylpiperidin-4-yl)piperidin-4-yl)-5,6-dihydro-imidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one × 2 HCl
[M^+ = 369]

Example 31
2-[(*Z*)-1-(4-Fluorophenyl)-2-(pyridin-3-yl)ethenyl]-5,6-dihydro-imidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+ = 384]

Example 32
2-(1-Benzylpiperidin-3-yl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]-benzodiazepin-7(4*H*)-one
[M^+ = 360]

Example 33
2-(1-Phenylcyclopent-1-yl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]-benzodiazepin-7(4*H*)-one
[M^+ = 331]

Example 34
2-(1-Phenylcyclohex-1-yl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]-benzodiazepin-7(4*H*)-one
[M^+ = 345]

Example 35
6-(4-(Aminomethyl)cyclohex-1-yl)-5,6-dihydroimidazo[4,5,1-*jk*]-[1,4]benzodiazepin-7(4*H*)-one
[M^+ = 298]

Example 36
2-[(*E*)-2-(Pyridin-4-yl)ethenyl]-5,6-dihydroimidazo[4,5,1-*jk*]-[1,4]benzodiazepin-7(4*H*)-one
[M^+ = 290]

Example 37
2-[3-Cyanophenyl]-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4H)-one
[M^+-1 = 288]

Example 38
2-(2-Phenyl-1*H*-imidazol-4-yl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]-benzodiazepin-7(4*H*)-one
[M^+-1 = 329]

Example 39
2-[2-(4-Methylphenyl)-1,3-oxazol-4-yl]-5,6-dihydroimidazo-[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 344]

Example 40
2-[1-(4-Fluorophenyl)-5-methyl-1*H*-pyrazol-4-yl]-5,6-dihydro-imidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 361]

Example 41
2-[1-(4-Chlorophenyl)-1*H*-pyrazol-5-yl]-5,6-dihydroimidazo-[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 363]

Example 42
2-(3-Propyl-5-isoxazolyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]-benzodiazepin-7(4*H*)-one
[M^+-1 = 296]

Example 43
2-[1-(4-Methoxyphenyl)-1*H*-pyrrol-3-yl]-5,6-dihydroimidazo-[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 358]

Example 44
2-(1,2,5-Trimethyl-1*H*-pyrrol-3-yl)-5,6-dihydroimidazo-[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 294]

Example 45
2-(4-Benzoyl-1-methyl-1*H*-pyrrol-2-yl)-5,6-dihydroimidazo-[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 370]

Example 46
2-{4-Methyl-5-[4-(trifluoromethyl)phenyl]-3-isoxazolyl}-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 412]

Example 47
2-(5-Methyl-2-furyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 267]

Example 48
2-[1-(2-Chlorophenyl)-5-(trifluoromethyl)-1*H*-pyrazol-4-yl]-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 431]

Example 49
2-(5-Methyl-1*H*-imidazol-4-yl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]-benzodiazepin-7(4*H*)-one
[M^+-1 = 267]

Example 50
2-(1-Methyl-1*H*-pyrazol-4-yl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]-benzodiazepin-7(4*H*)-one
[M^+-1 = 267]

Example 51
2-(1-Methyl-1*H*-indol-3-yl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]-benzodiazepin-7(4*H*)-one
[M^+-1 = 316]

Example 52
2-{6-[(4-Chlorophenyl)thio]imidazo[2,1-*b*][1,3]thiazol-5-yl}-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 451]

Example 53
2-[1-(4-Chlorophenyl)-1*H*-pyrrol-3-yl]-5,6-dihydroimidazo-[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 363]

Example 54
2-[2-(4-Fluorobenzoyl)-1-benzofuran-5-yl]-5,6-dihydroimidazo-[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 425]

Example 55
2-(2,5-Dibromo-3-thienyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 427]

Example 56
2-(2-Phenyl-1,3-oxazol-4-yl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]-benzodiazepin-7(4*H*)-one
[M^+-1 = 330]

Example 57
2-(6-Methyl-2-pyridinyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 278]

Example 58
2-(1,5-Dimethyl-3-oxo-2-phenyl-2,3-dihydro-1*H*-pyrazol-4-yl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 373]

Example 59
2-[1-(Benzylaminocarbonylmethyl)pyrrol-2-yl]-5,6-dihydroimidazo-[4,5,1-jk][1,4]-benzodiazepin-7(4H)-one
[M^+-1 = 399]

Example 60
2-(1-Phenyl-1*H*-pyrazol-4-yl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]-benzodiazepin-7(4*H*)-one
[M^+-1 = 329]

Example 61
2-[1-(3-Cyano-4-methoxypyridin-2-yl)pyrrol-2-yl]-5,6-dihydro-imidazo[4,5,1-*jk*][1,4]-benzodiazepin-7(4H)-one
[M^+-1 = 384]

Example 62
2-{1-[(4-Methylphenyl)sulfonyl]-1*H*-indol-3-yl}-5,6-dihydro-imidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 456]

Example 63
2-(5-Methoxy-1*H*-indol-3-yl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]-benzodiazepin-7(4*H*)-one
[M^+-1 = 332]

Example 64
2-[4-Bromo-1-(4-chlorobenzyl)-1*H*-pyrazol-5-yl]-5,6-dihydro-imidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 456]

Example 65
2-[1-(4-Methylphenyl)-1*H*-pyrrol-2-yl]-5,6-dihydroimidazo-[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 342]

Example 66
2-(5-Chloro-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)-5,6-dihydro-imidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 377]

Example 67
2-[4-(4-Chlorobenzoyl)-1-methyl-1*H*-pyrrol-2-yl]-5,6-dihydro-imidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 404]

Example 68
2-[4-(Diethylamino)phenyl]-5,6-dihydroimidazo[4,5,1-*jk*][1,4]-benzodiazepin-7(4*H*)-one
[M^+-1 = 334]

Example 69
2-(4-Methoxy-1-naphthyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzo-diazepin-7(4*H*)-one
[M^+-1 = 343]

Example 70
2-(4-Methoxy-2,5-dimethylphenyl)-5,6-dihydroimidazo[4,5,1-*jk*]-[1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 321]

Example 71
2-[3-(4-Chlorophenoxy)phenyl]-5,6-dihydroimidazo[4,5,1-*jk*][1,4]-benzodiazepin-7(4*H*)-one
[M^+-1 = 389]

Example 72
2-[4-(Methylthio)phenyl]-5,6-dihydroimidazo[4,5,1-*jk*][1,4]-benzodiazepin-7(4*H*)-one
[M^+-1 = 309]

Example 73
2-[4-(Acetyloxy)phenyl]-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4H)-one
[M^+-1 = 321]

Example 74
2-[2,5-Bis(trifluoromethyl)phenyl]-5,6-dihydroimidazo[4,5,1-*jk*]-[1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 399]

Example 75
2-(2,3-Dimethoxyphenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 323]

Example 76
2-(2-Methylphenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 277]

Example 77
2-[4-(Benzyloxy)phenyl]-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 369]

Example 78
2-(2-Chloro-6-fluorophenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]-benzodiazepin-7(4*H*)-one
[M^+-1 = 315]

Example 79
2-(2-Ethoxyphenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 307]

Example 80
2-(4-Isopropylphenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 305]

Example 81
2-(6-Nitro-1,3-benzodioxol-5-yl)-5,6-dihydroimidazo[4,5,1-*jk*]-[1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 352]

Example 82
2-(2,3-Dihydro-1,4-benzodioxin-6-yl)-5,6-dihydroimidazo-[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 321]

Example 83
2-[4-(Dimethylamino)-1-naphthyl]-5,6-dihydroimidazo[4,5,1-*jk*]-[1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 355]

Example 84
2-[4-(Difluoromethoxy)phenyl]-5,6-dihydroimidazo[4,5,1-*jk*][1,4]-benzodiazepin-7(4*H*)-one
[M^+-1 = 329]

Example 85
2-(3,7-Dichloro-8-quinolinyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]-benzodiazepin-7(4*H*)-one
[M^+-1 = 383]

Example 86
2-[4-Chloro-3-(trifluoromethyl)phenyl]-5,6-dihydroimidazo-[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 365]

Example 87
2-(1-*tert*-Butyl-1*H*-pyrazol-4-yl)-5,6-dihydroimidazo[4,5,1-*jk*]-[1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 309]

Example 88
2-(4-Chloro-5-nitro-1-benzothien-2-yl)-5,6-dihydroimidazo-[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 398]

Example 89
2-[1-(4-Phthalimidobutan-1-yl)indol-3-yl]-5,6-dihydroimidazo-[4,5,1-*jk*][1,4]benzodiazepin-7(4H)-one
[M^+-1 = 503]

Example 90
2-(3-Isobutyl-5-isoxazolyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]-benzodiazepin-7(4*H*)-one
[M^+-1 = 310]

Example 91
2-[1-(4-Methoxyphenyl)-5-(trifluoromethyl)-1*H*-pyrazol-4-yl]-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 427]

Example 92
2-[2-(Dimethylamino)-1,3-thiazol-5-yl]-5,6-dihydroimidazo-[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 313]

Example 93
2-[3-(4-*tert*-Butylphenyl)-5-isoxazolyl]-5,6-dihydroimidazo-[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 386]

Example 94
2-[1-(4-Chlorophenyl)-3,5-dimethyl-1*H*-pyrazol-4-yl]-5,6-dihydro-imidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 391]

Example 95
2-(3-Chlorophenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzo-diazepin-7(4*H*)-one
[M^+-1 = 297]

Example 96
2-(3-Fluorophenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 281]

Example 97
2-(3-Phthalimidophenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzo-diazepin-7(4H)-one
[M^+-1 = 408]

Example 98
2-{4-[3-Chloro-5-(trifluoromethyl)-2-pyridinyl]phenyl}-5,6-di-hydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 442]

Example 99
2-[5-(6-Methylnicotinamido)-2-chlorophenyl]-5,6-dihydroimidazo-[4,5,1-jk][1,4]-benzodiazepin-7(4H)-one
[M^+-1 = 431]

Example 100
2-(4-*tert*-Butoxyphenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 335]

Example 101
4-(7-Oxo-4,5,6,7-tetrahydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-2-yl)benzonitrile
[M^+-1 = 288]

Example 102
2-[3-(Trifluoromethoxy)phenyl]-5,6-dihydroimidazo[4,5,1-*jk*][1,4]-benzodiazepin-7(4*H*)-one
[M^+-1 = 347]

Example 103
2-[3-(3,5-Dichlorophenoxy)phenyl]-5,6-dihydroimidazo[4,5,1-*jk*]-[1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 423]

Example 104
2-(3-Bromo-4,5-dimethoxyphenyl)-5,6-dihydroimidazo[4,5,1-*jk*]-[1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 402]

Example 105
2-[5-(Allyloxy)-1,3-dimethyl-1*H*-pyrazol-4-yl]-5,6-dihydroimidazo-[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 337]

Example 106
2-{2-[3-(Trifluoromethyl)anilino]phenyl}-5,6-dihydroimidazo-[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 422]

Example 107
2-[2-(2-Phenylethyl)phenyl]-5,6-dihydroimidazo[4,5,1-*jk*][1,4]-benzodiazepin-7(4*H*)-one
[M^+-1 = 367]

Example 108
2-(3-Benzoylphenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 367]

Example 109
2-(4-Acetamidophenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzo-diazepin-7(4H)-one
[M^+-1 = 320]

Example 110
2-(1,3-Benzodioxol-5-yl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzo-diazepin-7(4*H*)-one
[M^+-1 = 307]

Example 111
2-(5-Aminosulfonyl-2,4-dichlorophenyl)-5,6-dihydroimidazo-[4,5,1-*jk*]-[1,4]benzodiazepin-7(4H)-one
[M^+-1 = 411]

Example 112
2-(2-Benzoyloxymethylphenyl)-5,6-dihydroimidazo[4,5,1-*jk*]-[1,4]benzodiazepin-7(4H)-one
[M^+-1 = 397]

Example 113
2-(2-N,N-Diethylaminocarbonyl-3,6-difluor-phenyl)-5,6-dihydro-imidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M^+-1 = 398]

Example 114
2-(2-(N-2,2,2-Trifluoracetamido)phenyl)-5,6-dihydroimidazo-[4,5,1-*jk*]-[1,4]benzodiazepin-7(4H)-one
[M^+-1 = 374]

Example 115
2-[4-(Trifluoromethyl)phenyl]-5,6-dihydroimidazo[4,5,1-*jk*][1,4]-benzodiazepin-7(4*H*)-one
[M^+-1 = 331]

Example 116
2-[2-Fluoro-4-(trifluoromethyl)phenyl]-5,6-dihydroimidazo-[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 349]

Example 117
2-(3-Chloro-4-methoxyphenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]-benzodiazepin-7(4*H*)-one
[M^+-1 = 327]

Example 118
2-(3-Bromo-4-fluorophenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]-benzodiazepin-7(4*H*)-one
[M^+-1 = 360]

Example 119
2-(2,5-Dimethyl-1-phenyl-1*H*-pyrrol-3-yl)-5,6-dihydroimidazo-[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 356]

Example 120
2-[4-(2,4-Dichlorobenzoyl)-1-methyl-1*H*-pyrrol-2-yl]-5,6-dihydro-imidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 439]

Example 121
2-[1-(2-Fluorophenyl)-1*H*-pyrrol-2-yl]-5,6-dihydroimidazo-[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 346]

Example 122
2-(3,5-Dimethoxyphenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzo-diazepin-7(4*H*)-one
[M^+-1 = 323]

Example 123
2-(4-Bromo-2-fluorophenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]-benzodiazepin-7(4*H*)-one
[M^+-1 = 360]

Example 124
2-(2-Chloro-4-fluorophenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]-benzodiazepin-7(4*H*)-one
[M^+-1 = 315]

Example 125
2-[2-(Benzyloxy)-3-methoxyphenyl]-5,6-dihydroimidazo[4,5,1-*jk*]-[1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 399]

Example 126
2-(2,4-Diethoxy-3-methylphenyl)-5,6-dihydroimidazo[4,5,1-*jk*]-[1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 365]

Example 127
2-(5-Bromo-2,4-dimethoxyphenyl)-5,6-dihydroimidazo[4,5,1-*jk*]-[1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 402]

Example 128
2-[4-(Dimethylamino)-2-methoxyphenyl]-5,6-dihydroimidazo-[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 336]

Example 129
2-[2-Chloro-5-(trifluoromethyl)phenyl]-5,6-dihydroimidazo-[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 366]

Example 130
2-(3,5-Dimethylphenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzo-diazepin-7(4*H*)-one
[M^+-1 = 291]

Example 131
2-[4-Fluoro-2-(trifluoromethyl)phenyl]-5,6-dihydroimidazo-[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 349]

Example 132
2-(5-Bromo-2-fluorophenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]-benzodiazepin-7(4*H*)-one
[M^+-1 = 360]

Example 133
2-[4-(1-Pyrrolidinyl)phenyl]-5,6-dihydroimidazo[4,5,1-*jk*]-[1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 332]

Example 134
2-(4-Isopropoxyphenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzo-diazepin-7(4*H*)-one
[M^+-1 = 321]

Example 135
2-(3,5-Dibromophenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzo-diazepin-7(4*H*)-one
[M^+-1 = 421]

Example 136
2-[4-(Benzyloxy)-2-methoxyphenyl]-5,6-dihydroimidazo[4,5,1-*jk*]-[1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 399]

Example 137
2-[3-Fluoro-4-(trifluoromethyl)phenyl]-5,6-dihydroimidazo-[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 349]

Example 138
2-[5-(4-Nitrophenyl)-2-furyl]-5,6-dihydroimidazo[4,5,1-*jk*]-[1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 374]

Example 139
2-(3-Acetyloxyphenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzo-diazepin-7(4H)-one
[M^+-1 = 321]

Example 140
2-[2-(*tert*-Butylthio)phenyl]-5,6-dihydroimidazo[4,5,1-*jk*]-[1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 351]

Example 141
2-[2-Fluoro-5-(trifluoromethyl)phenyl]-5,6-dihydroimidazo-[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 349]

Example 142
2-(3,4-Dimethylphenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzo-diazepin-7(4*H*)-one
[M^+-1 = 291]

Example 143
2-[4-(Ethylthio)phenyl]-5,6-dihydroimidazo[4,5,1-*jk*][1,4]-benzodiazepin-7(4*H*)-one
[M^+-1 = 323]

Example 144
2-{4-[(Trifluoromethyl)thio]phenyl}-5,6-dihydroimidazo-[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 363]

Example 145
2-{2-[(4-Chlorophenyl)thio]phenyl}-5,6-dihydroimidazo-[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 406]

Example 146
2-(4-Chloro-3-fluorophenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]-benzodiazepin-7(4*H*)-one
[M^+-1 = 316]

Example 147
2-(2-(4-Ethoxycarbonyl-piperidin-1-yl)-thiazol-5-yl)-5,6-dihydro-imidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4H)-one
[M^+-1 = 425]

Example 148
2-{1,3-Dimethyl-5-[4-(trifluoromethyl)phenoxy]-1*H*-pyrazol-4-yl}-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 441]

Example 149
2-{1-Methyl-3-(trifluoromethyl)-5-[3-(trifluoromethyl)phenoxy]-1*H*-pyrazol-4-yl}-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 495]

Example 150
2-[2-(4-Benzyl-1-piperazinyl)-1,3-thiazol-5-yl]-5,6-dihydro-imidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 444]

Example 151
2-(5-Isopropyl-2-methylcyclohexyl)-5,6-dihydroimidazo[4,5,1-*jk*]-[1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 325]

Example 152
2-(6,6-Dimethylbicyclo[3.1.1]hept-2-yl)-5,6-dihydroimidazo-[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 309]

Example 153
2-[5-(3-Nitrophenyl)-2-furyl]-5,6-dihydroimidazo[4,5,1-*jk*][1,4]-benzodiazepin-7(4*H*)-one
[M^+-1 = 374]

Example 154
2-(2,5-Dimethoxytetrahydro-3-furanyl)-5,6-dihydroimidazo-[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 317]

Example 155
2-(2-Thienyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 269]

Example 156
2-(1,3-Thiazol-2-yl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzo-diazepin-7(4*H*)-one
[M^+-1 = 270]

Example 157
2-(4-Methoxycyclohexyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzo-diazepin-7(4*H*)-one
[M^+-1 = 299]

Example 158
2-(3,5-Dimethoxy-2-methoxycarbonylphenyl)-5,6-dihydroimidazo-[4,5,1-*jk*][1,4]benzodiazepin-7-(4H)-one
[M^+-1 = 381]

Example 159
2-{5-[1-Methyl-3-(trifluoromethyl)-1*H*-pyrazol-5-yl]-2-thienyl}-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 417]

Example 160
2-(2-Fluoro-5-methoxyphenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]-benzodiazepin-7(4*H*)-one
[M^+-1 = 311]

Example 161
2-(4-Butylphenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 319]

Example 162
2-[2-(Trifluoromethoxy)phenyl]-5,6-dihydroimidazo[4,5,1-*jk*][1,4]-benzodiazepin-7(4*H*)-one
[M^+-1 = 347]

Example 163
2-(4-Quinolinyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 314]

Example 164
2-(2-Quinolinyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 314]

Example 165
2-(2-Chloro-3-quinolinyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 348]

Example 166
2-[4-(1*H*-Pyrrol-1-yl)phenyl]-5,6-dihydroimidazo[4,5,1-*jk*][1,4]-benzodiazepin-7(4*H*)-one
[M^+-1 = 328]

Example 167
2-(1*H*-Indol-6-yl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 302]

Example 168
2-[4-(1,1-Dioxo-1,2-thiazinan-2-yl)-phenyl]-5,6-dihydroimidazo-[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 396]

Example 169
2-(1,3-Benzothiazol-6-yl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 320]

Example 170
2-(2,3-Dihydro-1-benzofuran-5-yl)-5,6-dihydroimidazo[4,5,1-*jk*]-[1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 305]

Example 171
2-(4-(2-(2-Furylmethylthio)acetamido)phenyl)-5,6-dihydroimidazo-[4,5,1-*jk*][1,4]benzodiazepin-7(4H)-one
[M^+-1 = 432]

Example 172
2-{[5-(2-Fluorobenzoyl)-2-thienyl]methyl}-5,6-dihydroimidazo-[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 405]

Example 173
2-(2-(2-Acetamidopyridin-5-ylthio)pyridin-5-yl)-5,6-dihydro-imidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M^+-1 = 430]

Example 174
2-(4-(N-(3,4-Dioxo-2-ethoxy-1-cyclobuten-1-yl)amino)phenyl-5,6-dihydroimidazo[4,5,1-*jk*][1,4]-benzodiazepin-7(4H)-one
[M^+-1 = 402]

Example 175
2-[(2-Quinoxalinylthio)methyl]-5,6-dihydroimidazo[4,5,1-*jk*]-[1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 361]

Example 176
2-[4-(Methylamino)phenyl]-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzo-diazepin-7(4*H*)-one
[M^+-1 = 292]

Example 177
2-(5-(4-Aminosulfonylphenyl)furan-2-yl)-5,6-dihydroimidazo-[4,5,1-*jk*][1,4]benzodiazepin-7(4H)-one
[M^+-1 = 408]

Example 178
2-{2,5-Dimethyl-1-[4-(trifluoromethyl)phenyl]-1*H*-pyrrol-3-yl}-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 424]

Example 179
2-{1-[(2,4-Difluorophenyl)sulfonyl]-1*H*-pyrrol-2-yl}-5,6-dihydro-imidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 428]

Example 180
2-{1-[2,6-Dichloro-4-(trifluoromethyl)phenyl]-2,5-dimethyl-1*H*-pyrrol-3-yl}-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 493]

Example 181
2-[5-(Phenylethynyl)-2-thienyl]-5,6-dihydroimidazo[4,5,1-*jk*]-[1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 369]

Example 182
2-{5-[2-(Trifluoromethoxy)phenyl]-2-furyl}-5,6-dihydroimidazo-[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 413]

Example 183
2-(5-(2-Methoxycarbonylthiophen-3-yl)furan-2-yl)-5,6-dihydro-imidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4H)-one
[M^+-1 = 393]

Example 184
2-(2,5-Dimethylphenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzo-diazepin-7(4*H*)-one
[M^+-1 = 291]

Example 185
2-(4-Methoxycarbonylphenyl)-5,6-dihydroimidazo[4,5,1-*jk*]-[1,4]benzodiazepin-7(4H)-one
[M^+-1 = 321]

Example 186
2-(4-Methylphenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzo-diazepin-7(4*H*)-one
[M^+-1 = 277]

Example 187
2-(3,4-Difluorophenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzo-diazepin-7(4*H*)-one
[M^+-1 = 299]

Example 188
2-(4-Fluorophenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzo-diazepin-7(4*H*)-one
[M^+-1 = 281]

Example 189
2-(3-Chloro-4-fluorophenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]-benzodiazepin-7(4*H*)-one
[M^+-1 = 315]

Example 190
2-(3-Bromo-4-methoxyphenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]-benzodiazepin-7(4*H*)-one
[M^+-1 = 372]

Example 191
2-[4-(Trifluoromethoxy)phenyl]-5,6-dihydroimidazo[4,5,1-*jk*][1,4]-benzodiazepin-7(4*H*)-one
[M^+-1 = 374]

Example 192
2-(2,5-Difluorophenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzo-diazepin-7(4*H*)-one
[M^+-1 = 299]

Example 193
2-[4-(1,1,2,2-Tetrafluoroethoxy)phenyl]-5,6-dihydroimidazo-[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 379]

Example 194
2-[4-Fluoro-3-(trifluoromethyl)phenyl]-5,6-dihydroimidazo-[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 349]

Example 195
2-(4-Cyanophenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzo-diazepin-7(4H)-one
[M^+-1 = 288]

Example 196
2-(3-Bromo-4-fluorophenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]-benzodiazepin-7(4*H*)-one
[M^+-1 = 360]

Example 197
2-(4-*tert*-Butyl-2-methylphenyl)-5,6-dihydroimidazo[4,5,1-*jk*]-[1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 333]

Example 198
2-[4-(1-Methoxy-1-methylethyl)phenyl]-5,6-dihydroimidazo-[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 335]

Example 199
2-(4-Bromophenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 342]

Example 200
2-[4-(3,4-Dichlorophenoxy)phenyl]-5,6-dihydroimidazo[4,5,1-*jk*]-[1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 424]

Example 201
2-[4-(2-Propynyloxy)phenyl]-5,6-dihydroimidazo[4,5,1-*jk*][1,4]-benzodiazepin-7(4*H*)-one
[M^+-1 = 317]

Example 202
2-{4-[Chloro(difluoro)methyl]phenyl}-5,6-dihydroimidazo-[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 347]

Example 203
2-(4-Benzoylphenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzo-diazepin-7(4*H*)-one
[M^+-1 = 367]

Example 204
2-(4-Ethylphenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 291]

Example 205
2-(2-Hydroxy-5-methylphenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]-benzodiazepin-7(4*H*)-one
[M^+-1 = 293]

Example 206
2-[4-(2,6-Difluorobenzoyl)-1-methyl-1*H*-pyrrol-2-yl]-5,6-dihydro-imidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 406]

Example 207
2-[4-(3-Chlorobenzoyl)-1-methyl-1*H*-pyrrol-2-yl]-5,6-dihydro-imidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 404]

Example 208
2-(2-Ethoxy-1-naphthyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 357]

Example 209
2-[2-(Benzyloxy)-4,5-dimethoxyphenyl]-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 429]

Example 210
2-{4-[(2-Chloroethyl)(ethyl)amino]-2-methylphenyl}-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 382]

Example 211
2-(4,5-Dimethoxy-2-methylphenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 337]

Example 212
2-(7-Methyl-2-naphthyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 327]

Example 213
2-(2,4-Dimethoxy-5-methylphenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 337]

Example 214
2-(3-Benzoyl-2,4-dichlorophenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 436]

Example 215
2-(6-Chloro-1,3-benzodioxol-5-yl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 341]

Example 216
2-[4-(Benzyloxy)-3,5-dimethoxyphenyl]-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 429]

Example 217
2-(3,4-Diethoxyphenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 351]

Example 218
2-(2-((Pyridin-2-yl)aminocarbonyl)eth-1-yl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4H)-one
[M^+-1 = 335]

Example 219
2-(3-((Pyridin-2-yl)aminocarbonyl)prop-1-yl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4H)-one
[M^+-1 = 349]

Example 220
2-((1,3-Dimethyl-3,7-dihydro-2,6-dioxo-1H-purin-8-yl)methyl-5,6-dihydroimidazo[4,5,1-*jk*]-[1,4]benzodiazepin-7(4H)-one
[M^+-1 = 379]

Example 221
2-(2-((Thiazol-2-yl)aminocarbonyl)eth-1-yl)-5,6-dihydroimidazo-[4,5,1-*jk*][1,4]benzodiazepin-2-yl)-7(4H)-one
[M^+-1 = 341]

Example 222
2-{2-[(1,3-Dimethyl-1*H*-pyrazol-5-yl)amino]phenyl}-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 372]

Example 223
2-(2-(4-Chlorophenyl)methylthio-3-cyanopyridin-6-yl)-5,6-dihydroimidazo-[4,5,1-*jk*][1,4]benzodiazepin-7(4H)-one
[M^+-1 = 445]

Example 224
2-(4-tert-Butylphenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 319]

Example 225
2-{2,5-Dimethyl-1-[3-(trifluoromethyl)phenyl]-1*H*-pyrrol-3-yl}-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 424]

Example 226
2-(5-Chloro-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)-5,6-dihydro-imidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 377]

Example 227
2-[2,5-Bis(trifluoromethyl)phenyl]-5,6-dihydroimidazo[4,5,1-*jk*]-[1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 399]

Example 228
2-[4-(4-*tert*-Butyl-1,3-thiazol-2-yl)phenyl]-5,6-dihydroimidazo-[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M^+-1 = 402]

Example 229
2-(3-Cyano-4-N,N-dimethylamino-2-fluorophenyl)-5,6-dihydro-imidazo-[4,5,1-*jk*][1,4]benzodiazepin-7(4H)-one
[M^+-1 = 349]

Example 230
2-(6-Methoxy-2-naphthyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzo-diazepin-7(4*H*)-one
[M^+-1 = 343]

Example 231
2-(4-Isobutylphenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzo-diazepin-7(4*H*)-one
[M^+-1 = 319]

Example 232
2-(3-Bromo-4-methoxyphenyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]-benzodiazepin-7(4*H*)-one
[M^+-1 = 372]

The following compounds according to the invention can be prepared in analogy to the methods described above:

1. 2-(4-(4-n-propylpiperazin-1-yl)phenyl)-5,6-dihydroimidazo-[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

2. 2-(4-(4-isopropylpiperazin-1-yl)phenyl)-5,6-dihydroimidazo-[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

3. 2-(4-(4-benzylpiperazin-1-yl)phenyl)-5,6-dihydroimidazo-[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

4. 2-(4-(4-n-butylpiperazin-1-yl)phenyl)-5,6-dihydroimidazo-[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

5. 2-(4-(4-ethylpiperazin-1-yl)phenyl)-5,6-dihydroimidazo-[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

6. 2-(4-(2-N,N-dimethylaminoeth-1-yloxy)phenyl)-5,6-dihydro-imidazo[4,5,1-k][1,4]benzodiazepin-7(4H)-one

7. 2-(4-(2-pyrrolidin-1-yleth-1-yloxy)phenyl)-5,6-dihydroimid-azo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

8. 2-(4-(2-piperazin-1-yleth-1-yloxy)phenyl)-5,6-dihydro-imidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

9. 2-(4-(2-(4-methylpiperazin-1-yl)eth-1-yloxy)phenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

10. 2-(4-(2-(4-propylpiperazin-1-yl)eth-1-yloxy)phenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

11. 2-(4-(2-(4-ethylpiperazin-1-yl)eth-1-yloxy)phenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

12. 2-(4-(2-(4-benzylpiperazin-1-yl)eth-1-yloxy)phenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

13. 2-(4-(2-(4-acetamidopiperazin-1-yl)eth-1-yloxy)phenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

14. 2-(4-(2-(4-benzamidopiperazin-1-yl)eth-1-yloxy)phenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

15. 2-(4-(4-methylhomopiperazin-1-yl)phenyl)-5,6-dihydroimidazo-[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

16. 2-(4-(4-benzylhomopiperazin-1-yl)phenyl)-5,6-dihydroimidazo-[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

17. 2-(4-(4-n-butylhomopiperazin-1-yl)phenyl)-5,6-dihydro-imidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

18. 2-(4-(4-ethylhomopiperazin-1-yl)phenyl)-5,6-dihydroimidazo-[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

19. 2-(4-methoxyphenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

20. 2-(4-chlorophenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

21. 2-(4-aminophenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

22. 2-(4-isopropylphenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]-benzodiazepin-7(4H)-one

23. 2-(3-chlorophenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

24. 2-(3-methylphenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

25. 2-(3-phenylphenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

26. 2-(3-isopropylphenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]-benzodiazepin-7(4H)-one

27. 2-(3-fluorophenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

28. 2-piperidin-4-yl-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

29. 2-(1-ethylpiperidin-4-yl)-5,6-dihydroimidazo[4,5,1-jk]-[1,4]benzodiazepin-7(4H)-one

30. 2-(1-n-propylpiperidin-4-yl)-5,6-dihydroimidazo[4,5,1-jk]-[1,4]benzodiazepin-7(4H)-one

31. 2-(1-isopropylpiperidin-4-yl)-5,6-dihydroimidazo[4,5,1-jk]-[1,4]benzodiazepin-7(4H)-one

32. 2-pyridin-4-yl-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

33. 2-pyridin-2-yl-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

34. 2-thien-2-yl-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

35. 2-indol-5-yl-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

36. 2-indol-2-yl-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

37. 2-quinolin-3-yl-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

38. 2-isoquinolin-1-yl-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

39. 2-quinoxalin-2-yl-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

40. 2-naphth-2-yl-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

41. 2-(2-(N,N-dimethylamino)eth-1-ylamino)phenyl)-5,6-dihydroimidazo[4,5,1-k][1,4]benzodiazepin-7(4H)-one

42. 2-(2-(N,N-diethylamino)eth-1-ylamino)phenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

43. 2-(2-piperidin-1-yleth-1-ylamino)phenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

44. 2-(2-pyrrolidin-1-yleth-1-ylamino)phenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

45. 2-(3-(N,N-dimethylamino)prop-1-ylamino)phenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

46. 2-(3-(N,N-diethylamino)prop-1-ylamino)phenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

47. 2-(3-piperidin-1-ylprop-1-ylamino)phenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

48. 2-(3-pyrrolidin-1-ylprop-1-ylamino)phenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

49. 2-cyclohexyl-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

50. 2-(cis-4-aminocyclohex-1-yl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

51. 2-(4-methoxycyclohex-1-yl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

52. 2-phenyl-5,6-dihydroimidazo[5,4,1-*jk*][1,4]benzodiazepin-7(4*H*)-one

53. 2-(3-aminophenyl)-5,6-dihydroimidazo[5,4,1-*jk*][1,4]benzodiazepin-7(4*H*)-one

54. 2-(4-*N*,*N*-dimethylaminomethylphenyl)-5,6-dihydroimidazo[5,4,1-*jk*][1,4]benzodiazepin-7(4*H*)-one

55. 2-(4-(2-*N*,*N*-dimethylaminoeth-1-yl)phenyl)-5,6-dihydroimidazo[5,4,1-*jk*][1,4]benzodiazepin-7(4*H*)-one

56. 2-(4-hydroxyphenyl)-5,6-dihydroimidazo[5,4,1-*jk*][1,4]benzodiazepin-7(4*H*)-one

57. 2-(4-pyrrolidinemethylphenyl)-5,6-dihydroimidazo[5,4,1-*jk*][1,4]benzodiazepin-7(4*H*)-one

58. 2-(2-methylthiophenyl)-5,6-dihydroimidazo[5,4,1-*jk*][1,4]-benzodiazepin-7(4*H*)-one

59. 2-(4-carboxyphenyl)-5,6-dihydroimidazo[5,4,1-*jk*][1,4]benzodiazepin-7(4*H*)-one

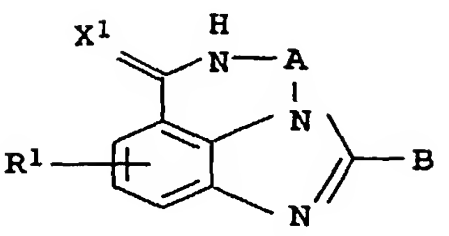
60. 2-(3,5-bis(trifluoromethyl)phenyl)-5,6-dihydroimidazo[5,4,1-*jk*][1,4]benzodiazepin-7(4*H*)-one

61. 2-(4-*tert*-butylphenyl)-5,6-dihydroimidazo[5,4,1-*jk*][1,4]-benzodiazepin-7(4*H*)-one

62. 2-(3-(morpholin-4-ylmethyl)phenyl)-5,6-dihydroimidazo[5,4,1-*jk*][1,4]benzodiazepin-7(4*H*)-one

We claim:

1. A compound of the formula I



I

in which

A can be a C_1-C_3 chain where each carbon atom may also carry one or two of the following substituents: C_1-C_4-alkyl, OH, O-C_1-C_4-alkyl, COOH, COO-C_1-C_4-alkyl and phenyl or one C atom may also carry an =O group, and

X^1 can be S, O and NH, and

R^1 is hydrogen, chlorine, fluorine, bromine, iodine, branched and unbranched C_1-C_6-alkyl, OH, nitro, CF_3, CN, $NR^{11}R^{12}$, NH-CO-R^{13}, O-C_1-C_4-alkyl, where R^{11} and R^{12} are, independently of one another, hydrogen or C_1-C_4-alkyl, and R^{13} is hydrogen, C_1-C_4-alkyl, C_1-C_4-alkyl-phenyl or phenyl, and

B can be an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 15 carbon atoms, an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 14 carbon atoms and 0 to 5 nitrogen atoms, 0 to 2 oxygen atoms or 0 to 2 sulfur atoms, each of which may also be substituted by one R^4 and a maximum of 3 different or identical R^5 radicals, and one or two carbon or sulfur atoms may also carry one or two =O groups, or is a radical L_v-Y-M_w in which

L can be a straight-chain or branched, saturated or unsaturated carbon chain of 1 to 8 C atoms, it being possible for each carbon atom to be substituted by one or two R^4 radicals and a maximum of two different or identical R^5 radicals, and

M has, independently of L, the same meaning as L, and

Y is a bond, or can be S, O or NR^3, where R^3 can be hydrogen, branched and unbranched C_1-C_6-alkyl, C_1-C_4-alkyl-phenyl, phenyl, and

v can be 0 and 1, and

w can be 0 and 1, and

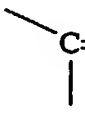
when Y is a bond, R^4 and R^5 are not both hydrogen, and

when B is L_v-Y-M_w, R^1 is not chlorine or NO_2, and

R^4 is hydrogen and $-(D)_p-(E)_s-(F^1)_q-G^1-(F^2)_r-(G^2)-G^3$, where

D can be S, NR^{43} and O

E can be phenyl,



$-SO_2-$, $-SO_2NH-$, $-NHCO-$, $-CONH-$, $NHSO_2-$, $-NHCOCH_2X^4$,

and

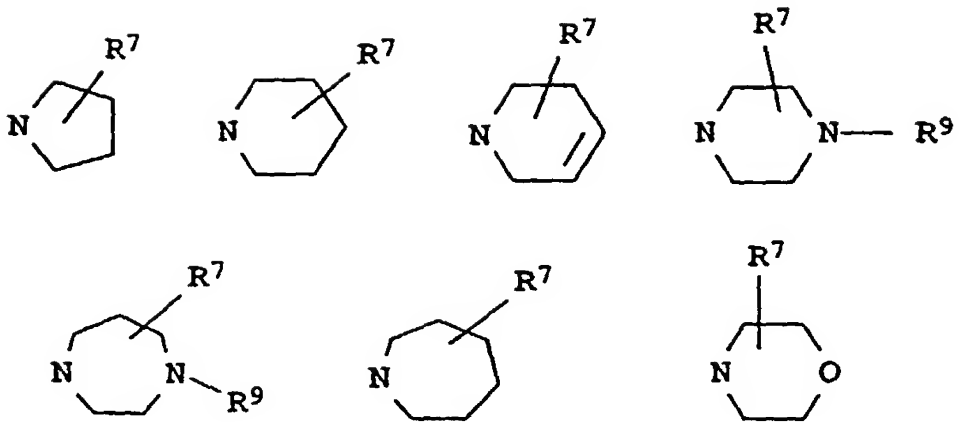
X^4 can be S, O or NH, and

F^1 can be a straight-chain or branched saturated or unsaturated carbon chain of 1 to 8 C atoms, and

F^2 has, independently of F^1, the same meaning as F^1,

G^1 is a bond or can be an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 15 carbon atoms, an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 14 carbon atoms and 0 to 5 nitrogen atoms, 0 to 2 oxygen atoms or 0 to 2 sulfur atoms, each of which may also be substituted by a maximum of 3 different or identical R^5 radicals, and one or two carbon or sulfur atoms may also carry one or two =O groups, and

G^2 is $NR^{41}R^{42}$ and



or a bond, and

G^3 can be an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 15 carbon atoms, an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 14 carbon atoms and 0 to 5 nitrogen atoms, 0 to 2 oxygen atoms or 0 to 2 sulfur atoms, each of which may also be substituted by a maximum of 3 different or identical radicals R^5, and one or two carbon or sulfur atoms may also carry one or two =O groups, or is hydrogen, and

p can be 0 and 1 and

s can be 0 and 1 and

q can be 0 and 1 and

r can be 0 and 1 and

R^{41} can be hydrogen, C_1-C_6-alkyl, it being possible for each carbon atom also to carry up to two R^6 radicals, phenyl which may also carry a maximum of two R^6 radicals, and $(CH_2)_t$-K and

R^{42} can be hydrogen, C_1-C_6-alkyl, -CO-R^8, CO_2-R^8, SO_2NH_2, SO_2-R^8, -(C=NH)-R^8 and -(C=NH)-NHR^8 and

R^{43} can be hydrogen and C_1-C_4-alkyl and

t can be 1, 2, 3, 4 and

K can be $NR^{11}R^{12}$, NR^{11}-C_1-C_4-alkyl-phenyl, pyrrolidine, piperidine, 1,2,5,6-tetrahydropyridine, morpholine, homopiperidine, piperazine, which may also be substituted

by an alkyl radical C_1-C_6-alkyl, and homopiperazine which may also be substituted by an alkyl radical C_1-C_6-alkyl, and

R^5 can be hydrogen, chlorine, fluorine, bromine, iodine, OH, nitro, CF_3, CN, $NR^{11}R^{12}$, NH-CO-R^{13}, C_1-C_4-alkyl-CO-NH-R^{13}, COR^8, C_0-C_4-alkyl-O-CO-R^{13}, C_1-C_4-alkyl-phenyl, phenyl, CO_2-C_1-C_4-alkyl, and branched and unbranched C_1-C_6-alkyl, O-C_1-C_4-alkyl, S-C_1-C_4-alkyl, it being possible for each C atom of the alkyl chains to carry up to two R^6 radicals, and for the alkyl chains also to be unsaturated, and,

R^6 can be hydrogen, chlorine, fluorine, bromine, iodine, branched and unbranched C_1-C_6-alkyl, OH, nitro, CF_3, CN, $NR^{11}R^{12}$, NH-CO-R^{13}, O-C_1-C_4-alkyl,

R^7 can be hydrogen, C_1-C_6-alkyl, phenyl, it being possible for the ring also to be substituted by up to two R^{71} radicals, and an amine $NR^{11}R^{12}$ or a cyclic saturated amine which has 3 to 7 members and may also be substituted by an alkyl radical C_1-C_6-alkyl, and homopiperazine which may also be substituted by an alkyl radical C_1-C_6-alkyl,

and where the radicals R^{11}, R^{12} and R^{13} in K, R^5, R^6 and R^7 may, independently of one another, assume the same meaning as for R^1, and

R^{71} can be OH, C_1-C_6-alkyl, O-C_1-C_4-alkyl, chlorine, bromine, iodine, fluorine, CF_3, nitro, NH_2, and

R^8 can be C_1-C_6-alkyl, CF_3, phenyl, C_1-C_4-alkyl-phenyl, it being possible for the ring also to be substituted by up to two R^{81} radicals, and

R^{81} can be OH, C_1-C_6-alkyl, O-C_1-C_4-alkyl, chlorine, bromine, iodine, fluorine, CF_3, nitro, NH_2, and

R^9 can be hydrogen, C_1-C_6-alkyl, C_1-C_4-alkyl-phenyl, CO_2-C_1-C_4-alkyl-phenyl, CO_2-C_1-C_4-alkyl, SO_2-phenyl, COR^8 and phenyl, it being possible for the phenyl rings also to be substituted by up to two R^{91} radicals, and

R^{91} can be OH, C_1-C_6-alkyl, O-C_1-C_4-alkyl, chlorine, bromine, iodine, fluorine, CF_3, nitro, NH_2,

and its tautomeric forms, possible enantiomeric and diastereomeric forms, and prodrugs thereof.

2. A compound of the formula I as claimed in claim 1, where

A is a C_2 chain, which may be substituted, and

X^1 is O, and

R^1 is hydrogen.

3. A compound of the formula I as claimed in either of claims 1 or 2, in which

B can be an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 15 carbon atoms, an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 14 carbon atoms and 0 to 5 nitrogen atoms, 0 to 2 oxygen atoms or 0 to 2 sulfur atoms, each of which may also be substituted by a maximum of 3 different or identical R^5 radicals, and one or two carbon or sulfur atoms may also carry one or two =O groups.

4. A compound of the formula I as claimed in claim 3, where

B is phenyl, cyclohexyl, piperidine, pyridine, pyrimidine, pyrrole, pyrazole, thiophene, furan, oxazole, naphthalene, piperazine, quinoline, pyrazine, each of which may also be substituted by one R^4 or a maximum of 2 R^5.

5. A compound of the formula I as claimed in claim 4, where

R^4 is hydrogen or $D_{0,1}$-$F^1{}_{0,1}$-G^2-G^3 with G^3 equal to hydrogen, and

D is O and NR^{43}, where R^{43} is hydrogen and C_1-C_3-alkyl and

F^1 is C_2-C_4-alkyl.

6. A compound of the formula I as claimed in either of claims 1 or 2, in which B is L_v-Y-M_w, where

v is 0, and

w is 1, and

Y is a bond, and

M can be a straight-chain or branched carbon chain of 2 to 8 C atoms which contains at least one double bond, it being possible for each carbon atom to be substituted by one or two R^4 radicals and a maximum of two different or identical R^5 radicals, and

R^1 is hydrogen, and

R^4 is $D_{0,1}$-$F^1{}_{0,1}$-G^1-G^2-G^3, with G^3 equal to hydrogen, and

D is O and NR^{43}, where R^{43} is hydrogen and C_1-C_3-alkyl and

F^1 is C_2-C_4-alkyl.

7. A drug comprising one or more compounds of the formula I as claimed in any of claims 1 to 6 in addition to conventional carriers and excipients.

8. The use of compounds of the formula I as claimed in any of claims 1 to 6 or of the formula I where R^1, X^1 and A have the meaning as above, and B can be hydrogen and a C_1-C_6-alkyl chain, for producing drugs with a PARP-inhibiting effect.

9. The use of compounds of the formula I as claimed in claim 8 for producing drugs for treating neurodegenerative disorders and neuronal damage.

10. The use as claimed in claim 8 for treating neurodegenerative disorders and neuronal damage caused by ischemia, trauma or massive bleeding.

11. The use as claimed in claim 8 for treating stroke and craniocerebral trauma.

12. The use as claimed in claim 8 for treating Alzheimer's disease, Parkinson's disease and Huntington's disease.

13. The use of compounds of the formula I as claimed in claim 8 for producing drugs for the treatment or prophylaxis of damage due to ischemias.

14. The use of compounds of the formula I as claimed in claim 8 for producing drugs for the treatment of epilepsies, in particular of generalized epileptic seizures, such as, for example, petit mal and tonoclonic seizures and partial epileptic seizures, such as temporal lobe, and complex partial seizures.

15. The use of compounds of the formula I as claimed in claim 8 for producing drugs for the treatment of damage to the kidneys after renal ischemia, damage caused by drug therapy such as, for example, during cyclosporin therapy, and for treatment during and after kidney transplants.

16. The use of compounds of the formula I as claimed in claim 8 for producing drugs for the treatment of damage to the heart following cardiac ischemia.

17. The use of compounds of the formula I as claimed in claim 8 for producing drugs for the treatment of microinfarcts such as, for example, during and after heart valve replacement, aneurysm resections and heart transplants.

18. The use of compounds of the formula I as claimed in claim 8 for producing drugs for treatment in cases of revascularization of critically narrowed coronary arteries such as, for example, in PTCA and bypass operations or of critically narrowed peripheral arteries, especially leg arteries.

19. The use of compounds of the formula I as claimed in claim 8 for producing drugs for the treatment of acute myocardial infarct and of damage during and after medical or mechanical lysis thereof.

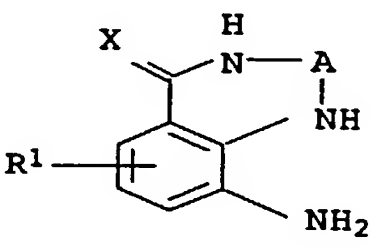
20. The use of compounds of the formula I as claimed in claim 8 for producing drugs for the treatment of tumors and metastasis thereof.

21. The use of compounds of the formula I as claimed in claim 8 for producing drugs for the treatment of sepsis, of multiorgan failure such as, for example, during septic shock and of acute respiratory distress syndrome.

22. The use of compounds of the formula I as claimed in claim 8 for producing drugs for the treatment of immunological disorders such as inflammations and rheumatic disorders such as, for example, rheumatoid arthritis.

23. The use of compounds of the formula I as claimed in claim 8 for producing drugs for the treatment of diabetes mellitus.

24. A compound of the formula III



III

in which

A is a C_1-C_3 chain it being possible for each carbon atom also to carry one or two of the following substituents: C_1-C_4-alkyl, OH, O-C_1-C_4-alkyl, CO_2H, CO_2-C_1-C_4-alkyl and phenyl or one C atom may also carry an =O group, and

X^1 and R^1 have the meanings stated in the previous claims,

excluding the compounds
9-amino-3-methyl-1,2,3,4-tetrahydro-5H-1,4-benzodiazepin-5-one,
9-amino-3-methyl-3,4-dihydro-1H-1,4-benzodiazepine-2,5-dione,
6,8-diamino-2,4-(1H,3H)-quinazolinedione,
8-amino-2,4-(1H,3H)-quinazolinedione,

and the salts thereof.

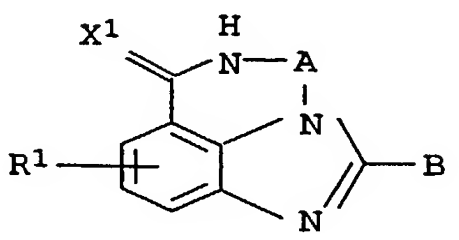
25. A process for preparing compounds of the formula III and salts thereof, wherein 2-halo-3-nitrobenzoic esters are reacted with a suitable diamine in a polar solvent in the presence of a base, and then the nitro group is hydrogenated with hydrogen in the presence of a suitable catalyst.

26. The use of compounds of the formula III in the synthesis of PARP inhibitors.

Benzodiazepine derivatives, the preparation and use thereof

Abstract

The invention relates to compounds of the formula I



I

and their tautomeric forms, possible enantiomeric and diastereomeric forms, and prodrugs thereof, the preparation and use thereof, where the values have the meaning stated in the description.

PT 90644 US - 0091 - 02.0050-05

DECLARATION AND POWER OF ATTORNEY

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

BENZODIAZEPINE DERIVATIVES, THE PREPARATION AND USE THEREOF

the specification of which:

[ ] is attached hereto.
[x] was filed as ~~10/088,604~~ as U.S. Application Serial No.
[X] was filed as PCT/EP00/09023 as PCT Application Serial No.

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

[ ] In compliance with this duty, attached is an information disclosure statement.

I acknowledge the duty to disclose information which is material to the examination of this application in accordance with Title 37, Code of Federal Regulations, § 1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, § 119 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed:

Prior Foreign Application(s)			Priority Claimed Yes	No
199 46 289.5	GERMANY	Sept. 28,1999	[ ]	[ ]
			[ ]	[ ]
			[ ]	[ ]
			[ ]	[ ]
Number	Country	Date Filed		

I hereby claim the benefit under Title 35, United States Code, § 120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, § 112, I acknowledge the duty to disclose material information as defined in Title 37, Code of Federal Regulations, § 1.56 which occurred between the filing date of the prior application and the national or PCT international filing date of this application:

[redacted]

Serial No. Date Status

I hereby appoint KEIL & WEINKAUF their attorneys and/or agents: Herbert B. Keil, Reg. No. 18,967; Russell E. Weinkauf, Reg. No. 18,495; Gerald H. Bjorge, Reg. No. 32,386; Norman G. Torchin, Reg. No. 34,068; Henry R. Jiles, Reg. No. 32,677; Jason D. Voight, Reg. No. 42,205; George F. Helfrich, Reg. No. 22,350; Ronald H. Smith, Reg. No. 43,679; David C. Liechty, Reg. No. 48,692, the address of all being KEIL & WEINKAUF, 1101 Connecticut Avenue, N.W., Suite 620, Washington, D.C. 20036 (telephone (202)659-0100), with full power to prosecute this application and transact all business in the Patent Office connected therewith.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

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Inventor's signature Date

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Inventor's signature Date

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Full name of eighth joint inventor, if any

Inventor's signature Date

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Full name of ninth joint inventor, if any

Inventor's signature Date